VOL. 48 NOVEMBER, 1954 No. 5

AMERICAN HEART JOURNAL

AN INTERNATIONAL PUBLICATION FOR THE STUDY OF THE CIRCULATION

Contents on Inside Cover

American Heart Journal

CONTENTS FOR NOVEMBER, 1954

Original Communications

Clinical Reports

Book Reviews

Announcement

Vol. 48, No. 5, November, 1954, American Heart Journal is published monthly, by The C. V. Mosby Company, 3207 Washington Avenue, St. Louis 3, Missouri, entered as second class matter January 23, 1917 at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Additional entry authorized at Jefferson City, Missouri. Subscription Price: United States, and its Possessions, per year $12.00; Canada $13.00; Foreign $13.50. Printed in the U. S. A.

American Heart Journal

VOL. 48 NOVEMBER, 1954 NO. 5

Original Communications

PSYCHOLOGICAL OBSERVATIONS OF PATIENTS UNDERGOING MITRAL SURGERY

A STUDY OF STRESS

HENRY M. FOX, M.D.,* NICHOLAS D. RIZZO, M.D.,** AND SANFORD GIFFORD, M.D.**

BOSTON, MASS.

PATIENTS undergoing mitral surgery provide an unusual opportunity for the study of acute and chronic stress. The various psychological responses of these patients to hospitalization and operation illustrate the effects of prolonged adaptation to an increasingly disabling disease which is followed by the hope of surgical rescue but also the chance of sudden death. All of these patients had, of course, been victims of rheumatic fever, and each had learned during the months or years before coming for operation that his heart had become diseased. He had also been warned, usually at a different time, by shortness of breath, palpitation, or an alarming episode of hemoptysis that the limits of his physical capacity were narrowing. This danger not only affected vital decisions concerning marriage, pregnancy, and choice of vocation but also influenced the intimate details of daily living, including the manner of walking, talking, and breathing. In carrying out an adjustment of such scope, the response of each patient was inevitably characterized by his individual mode of adaptation to the demands of reality and by the nature of his psychological defenses. Although the patient's

From the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Psychiatry, Harvard Medical School, Boston, Massachusetts.

*Physician, Peter Bent Brigham Hospital, and Assistant Professor of Psychiatry, Harvard Medical School.

**Associate in Psychiatry, Peter Bent Brigham Hospital, and Instructor in Psychiatry, Harvard Medical School.

This investigation has been supported in part by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-213; and in part by a grant from the Ford Foundation.

The authors wish to indicate their appreciation to Dr. Lewis Dexter, Dr. Dwight E. Harken and their associates at the Peter Bent Brigham Hospital for their interest and cooperation throughout the study.

We wish to extend our thanks to the Editor and publishers of *Psychosomatic Medicine* for their permission to publish the above paper by Drs. Henry M. Fox, Nicholas D. Rizzo, and Sanford Gifford, as we believe it will be of interest to the readers of this Journal. ED.

Reprinted from *Psychosomatic Medicine*, May-June, 1954.

sense of danger and his way of reacting to it may be determined to a large extent by the realities of the situation, his phantasies about his illness and about what might happen on the operating table also influence his feelings and his behavior. The following study demonstrates that an understanding of the long-term adaptation to progressive limitation of activities provides the necessary background for the recognition of emergency defenses as they develop in the hospital situation both before and after operation.

SETTING

The attention of the psychiatrists had first been attracted when consultations were requested on a number of patients who had developed depressive reactions of some severity following the operation. In order to avoid selection of the cases on the basis of obvious emotional disturbance, the attempt was made to interview—preoperatively and also postoperatively—every patient admitted to the hospital for consideration of mitral surgery. We therefore interviewed some patients who were discharged without operation (the disappointment in some instances constituted quite a severe stress), but we have limited the present study to patients who actually had the operation. In the six months between July 1 and December 31, 1951 (excluding the month of August), 50 patients at the Peter Bent Brigham Hospital had mitral surgery. Thirty-two of these were interviewed by the psychiatrists preoperatively and postoperatively and they constitute the basis for the present study. The remaining eighteen were seen only postoperatively or were not seen at all. This was more because the psychiatrists did not have time available for the interviews when informed of the patient's admission rather than because of any objection from the patients themselves (except in 1 case).

It was explained to the patients that a talk with the psychiatrist was part of the routine preoperative investigation and that we were interested in learning about how people had adjusted themselves to their illness, and how they felt about coming to the hospital for an operation of this sort. An occasional patient concluded that the interview with the psychiatrist might have a bearing on his candidacy for the operation, but in most instances the operation had already been decided upon by the time the psychiatric interview took place. The interviews were not presented as therapeutic in nature, even though many of the patients made therapeutic use of them, as described below.

Preoperative physiological studies, including cardiac catheterizations in some cases, were carried out under the supervision of Dr. Lewis Dexter, who collaborated closely with Dr. Dwight E. Harken, the surgeon. The patients were in the hospital for varying lengths of time preceding operation. The shortest time was 3 days and the longest 27 days. The average (median value) was 8 days. This was determined by how many of the physiological studies had been carried out prior to admission, the presence of complications such as fever which suggested the possibility of rheumatic activity, and the patient's general condition. The patients who survived remained in the hospital after operation for an average (median value) of 16 days. This was determined by the various factors affecting convalescence, including the severity of the cardiac disease (whether or not there was mitral insufficiency as well as mitral stenosis, the extent to which other valves might have been involved, and the presence of

rheumatic activity), the technical success of the operation, and the development of postoperative complications. The postoperative psychological factors will be discussed in more detail.

METHODS

The patients were seen in the psychiatrist's private office at the hospital. The three psychiatrists who participated in the study each saw a certain number of the patients. Most of them were seen only once or twice preoperatively. The last preoperative interview usually took place within 48 hours of the operation. Although many of the patients were seen briefly at the bedside within the first week after operation, they were not interviewed in the psychiatrist's office until 7 days postoperatively. The number of postoperative interviews varied from one to five or six. Complete tape recordings were made of all office interviews, each of which lasted from 30 to 50 minutes. All of these interviews were subsequently typewritten and were made available to the psychiatrists for review. This information was then condensed to the essential preoperative and postoperative observations. An interpretation of the psychological defenses illustrated by each case was then made on the basis of the patient's life history, the observations made in the hospital, and the available follow-up information (Table I).

During interviews the microphone was placed on the desk in plain view and the patient was told that the recording was being made. He was assured that the material would be treated confidentially and all identities have been protected in the present report. Only 2 of the patients objected to the recording. Out of the whole series they happened to be the 2 who had especially tried to conceal the fact that they had heart disease. One was a woman (Case 12) who expressed a feeling of suspicion about what might happen to the records. She had made sure that her employers did not know she had heart trouble and used to leave for work over an hour ahead of time so that she could walk slowly enough not to have anyone see that she was out of breath. She especially avoided physical examinations or an X-ray which would show her enlarged heart. The other patient was a man (Case 32) who rested the entire week end so that he could continue at work and not have anyone find out that he had heart disease. It later developed that in both patients the knowledge that there was something wrong with the heart was associated with a feeling of sexual inadequacy.

All three psychiatrists made use of the same interviewing technique, although there were, of course, individual variations. The method was, in general, an adaptation of the associative anamnesis as described by Felix Deutsch.[1] The psychiatrist tried as much as possible to allow the patient to make spontaneous comments about his past experiences and his present feelings. From time to time one of the patient's phrases was repeated questioningly as a stimulus for further associations. We tried to stay as close as possible to emotionally meaningful material which seemed to have a bearing on the patient's adjustment to the limitation of his activities or on his feelings and phantasies about the operation. Although we were often able to obtain interesting indications concerning the quality of the patient's relationships to members of his immediate family, we depended on the history as taken by the medical or surgical house officer for some of the factual material such as the ages of siblings, the ages and causes of death of various members of the family, and for the record of previous illnesses

TABLE I. TABULAR SUMMARY OF PATIENTS

CASE	PREOPERATIVE	POSTOPERATIVE	INTERPRETATION OF BACKGROUND	NO. OF DAYS IN HOSP. (POSTOP.) AND FOLLOW-UP
Case 1 Male: S Age: 25 MS II	Optimistic because God will decide.	Pleased with "sharp heart beat" instead of "sloppy thud." (*Fibrillation*)	Attempt to resolve feelings of rebellion and helplessness by submission to "God's will."	21 days 12 mos. p.o. After one month of marriage heart reported adequate for the "physical aspects thereof."
Case 2 Female: M Age: 36 MS III Sev. pulmonary vascular disease	Discouraged, "in a fog," and as if "can't hear."	Mild elation. Felt life starting over and expressed loving gratitude to surgeon. (*Fibrillation 5th—11th p.o. days, thrombophlebitis 9th day*)	Activity the alternative to womblike withdrawal and sense of vulnerability to possessive domination (by daughter).	16 days 12 mos. p.o. Feeling fine and doing well.
Case 3 Female: S Age: 36 MS III	Expressed religious zeal and described former business competence.	Frightened by unexpected pain (*pulmonary infarction*). Guilty that faith was not strong enough.	"Doing the Lord's work" the alternative to guilt and masochistic fears.	16 days 3 mos. p.o. Still having pain. Physician thought she was trying to do too much.
Case 4 Male: M Age: 42 MS III MI	Blustering and displaying big muscles.	Querulous complaining about cough, tubes in chest, and thumping sensations. (*Fibrillation*)	Dependence on narcissistic defenses (body pride).	15 days 2 mos. p.o. Feels fine but anxious about chest pain.
Case 5 Female: M Age: 45 MS IV	Talkative. Excited since acceptance as "candidate for surgery."	Elated and apparently unaware of pain. "Uncontrollable surge of energy."	Elation and hypomanic activity served to deny pain and fear.	13 days 15 mos. p.o. "Ashamed" to complain of pain. Finds it harder to convince herself that she is "up on pink cloud."

Case 6 Female: M Age: 37 RHD, active MS II MI (postop.)	Somewhat seductive. Described having taken good care of her body.	Complained insistently that nurses did not hear her, but very friendly to doctors. (*Transient fibrillation and fever*)	Narcissistic defenses (body care and glamorous clothing) against body damage. Infantile dependence (mother and sister are nurses).	18 days 10 mos. p.o. Menstruation improved. "Progressing from a passive spectator to a more active participant in life."
Case 7 Male: M Age: 32 MS III MI	Immobile, expressionless, fatalistic. Stressed his "normality" and absence of worry because of confidence in surgeon. (*Vagus release just prior to introduction venous catheter*)	Still immobile. Uneasy about supine position and insisted on sitting up. (*At operation: ventricular irritability and other arrhythmias; p.o.: Femoral embolus and right hemothorax*)	Denial of weakness by rigid immobility and surrender to "fate" after disease shook pride in physical prowess.	15 days 1 mo. p.o. Feels "marvelous" (said somberly). Attributes weakness to weight loss and salt-free diet.
Case 8 Female: W Age: 28 RHD, active MS III MI (postop.)	Confessed belief that she had brought heart trouble on herself by pretending she had it at age of 8. Felt "numb" preoperatively.	Felt "numb," "as though dead," and things seemed "unreal" until after diuresis on 3rd p.o. day. (*Hyponatremia and transfusion reaction*)	Depersonalization and unreality were hysterical defenses against frightening phantasies about the operation.	22 days 4 mos. p.o. "Eternally grateful" for the "wonderful miracle." 7 mos. p.o. "Too good to be true."
Case 9 Male: M Age: 46 MS III	Restless and lively. Would rather be dead than disabled.	Euphoric. Describes heart operation as touching "the most delicate thing a man has." (*Slightly disoriented while on bladder drainage for retention*)	Operation thought of as narrow escape from demasculinization.	20 days 11 mos. p.o. Swims, fishes, feels younger, flirts with girls, and sews neckties.
Case 10 Male: S Age: 49 MS III	Felt the Almighty calling and put himself in His hands.	Persisting amnesia for 3 p.o. days. "No heartache, no memory of pain."	Passive surrender to avoid the consequences of aggression.	15 days 7 mos. p.o. "Eternally obligated" to the surgeon.

TABLE I. TABULAR SUMMARY OF PATIENTS—(CONT'D)

CASE	PREOPERATIVE	POSTOPERATIVE	INTERPRETATION OF BACKGROUND	NO. OF DAYS IN HOSP. (POSTOP.) AND FOLLOW-UP
Case 11 Female: M Age: 33 MS IV	Frozen, expressionless and whispered almost inaudibly.	Amnesia for 3 p.o. days. Then spoke louder but told little. "Feels like it's a dream." (*Auricular tachycardia at operation*)	Immobilization and amnesia defensive against probable fears of disintegration.	14 days No information.
Case 12 Female: S Age: 32 MS III	Reluctant to talk. Had kept illness secret.	Crying spells and vomiting.	Substitution of illness for feelings of feminine inadequacy.	15 days 9 mos. p.o. Well except for fatigue and chest pain.
Case 13 Female: M Age: 29 MS III MI	Fearful of operation. Thought heart might stop beating.	Felt surgeon gave her a "new life"—"It's like a dream." (*Had cardiac standstill 6–10 minutes during operation*).	Recent marriage and present operation felt as separation from mother upon whom she had masochistic dependence.	15 days. 10 mos. p.o. Grateful for "this new life." Can hardly believe she is the same person.
Case 14 Female: M Age: 39 MS III	Talked incessantly and could not sit still. Guilty about illness. "Afraid I won't live . . . afraid they won't have me asleep."	Exhausted but alert. Died 18 hours p.o. (*Blood pressure unobtainable*)	Overactivity expressed guilt and terror of operation.	Died 18 hours p.o.
Case 15 Female: M Age: 37 MS III MI (postop.)	Took over interview. Stressed self-reliance and activity.	Tenacious struggle to regain speech and motor power. (*Cerebral embolus*)	Stress on activity rather than submission to "domineering" mother.	22 days 15 mos. p.o. All neurological function restored.

Case 16 Female: W Age: 37 MS III	Aggressive demands for help. Felt misinformed and mistreated.	Accentuation of pain and dependence on drugs.	Delusional projection and addiction tendency as expressions of demanding (regressive) dependence.	28 days 15 mos. p.o. Still on narcotic drugs.
Case 17 Female: M Age: 45 MS IV MI (lucite ball)	Aware of desperate physical plight and unafraid of operation.	Shock. Died 1 day p.o.	Overconfidence in operation as denial of death threat.	1 day Died 1 day p.o.
Case 18 Female: M Age: 34 MS III	Amused bitterness about disappointed ambitions. Expressed guilt and fatigue.	"Sometimes the only thing you know is pain. . . . Can't seem to navigate." *(? Splenic infarct 7 days p.o.)*	Active strivings replaced by resentment, guilt, and pain.	23 days 4 mos. p.o. "No ambition." "Not worth it." Very tired. 6 mos. p.o. Readmitted for incisional pain.
Case 19 Female: S Age: 43 RHD, active MS IV MI *CH*F (lucite ball)	Afraid of becoming a hopeless invalid, tired and depressed.	Feels surgeon "disappointed" in her. "Nothing to live for." *(Fever, cortisone therapy, progressive failure)*	Feels jilted by men who fail to rescue her from spinsterhood and hopeless dependence on mother.	45 days Died 45 days p.o.
Case 20 Male: S Age: 36 MS II AI	Suspicious of psychiatrist. Denied brooding about his disease.	Hostile and resentful. Amnesia for 3 days p.o. Visual impairment highly variable. *(Occipital lobe ischemia, atelectasis)*	Hysterical defense against possible development of paranoid panic.	21 days 3 mos. p.o. Vision markedly improved.
Case 21 Female: M Age: 45 MS III MI	Emphasized how active she had always been. Not afraid because the doctors are "wonderful."	"Even on the operating table I had no fear at all" but vomited and "could not eat" for 4 days afterwards.	Denies fear by infantile dependence on doctors' mothering care, but maintains active mothering role toward husband.	15 days 9 mos. p.o. Getting along very well. Heart feels "wonderful."

TABLE I. TABULAR SUMMARY OF PATIENTS—(CONT'D)

CASE	PREOPERATIVE	POSTOPERATIVE	INTERPRETATION OF BACKGROUND	NO. OF DAYS IN HOSP. (POSTOP.) AND FOLLOW-UP
Case 22 Female: S Age: 40 MS III	Vivacious and confident but preoccupied with deaths of father, brother, and recently, of mother.	Anxious awareness of struggle to regain consciousness. (*Ventricular tachycardia, hypotension*)	Active struggle against death wishes (? to be with mother).	17 days Grateful for "brand new heart."
Case 23 Female: M Age: 34 MS IV MI AF (lucite ball)	Jibing and joking that she would not be caught dead in Boston.	Not fully oriented. Died 16 days p.o. (*Hypotension, thrombophlebitis, hyponatremia, pulmonary embolism, increasing failure*)	Use of gallows humor to deny identification with mother who died of postoperative shock when exactly patient's present age.	16 days Died 16 days p.o.
Case 24 Female: M Age: 28 MS III	Articulate and outspoken. Feels choked, smothered with attention, and depressed.	Felt reborn.	Active and aggressive as protest against smothering dependence on mother.	23 days 7 mos. p.o. "Wonderful" except for occasional "pounding" when "frightened and insecure."
Case 25 Female: M Age: 42 MS II	Scared, thinks doctors cold blooded, but has absolute confidence in Drs. Dexter and Harken.	Felt operation "a miracle" but complains of pain and "disorganized" breathing.	Attempt to balance destructive by protective aspects of rescue. (Confidence in chief physicians)	14 days 3–5 mos. p.o. "State of mind" improved but "heart pounds." 7 mos. p.o. Rheumatic recurrence. "Morale hit bottom."
Case 26 Female: M Age: 31 RHD, active MS III	Explosive abreaction of past sexual experiences. Phantasied surgeon as "Svengali-like."	Hysterical hallucination of seeing psychiatrist in operating room who "would not let her die or be hurt."	Hysterical transference to psychiatrist as protection against terrifying phantasies of attack by surgeon.	19 days 5 mos. p.o. Doing well.

Case 27 Male: W Age: 44 MS IV MI	Booming voice despite wasted, skeleton-like appearance and vomiting.	Felt reborn. Became very dependent on younger brother. (*Fibrillation*)	Maintained aggressive activity by regressive dependence (on dead wife and then on younger brother).	16 days Remarried. Sent surgeon greeting card on Mother's Day signed "Your reborn son."
Case 28 Female: M Age: 39 MS IV MI AS AI	Threatened suicide as alternative to surgery.	Confessed stealing salt. Vomited, complained of pain, and "would not go through operation again." (*Auricular flutter, ? digitalis intoxication*)	Self-destructive (? identification with mother who recently died of cancer).	48 days Died 2-3 weeks after leaving hospital.
Case 29 Female: S Age: 29 MS IV MI (lucite ball)	Terrified of second operation.	Extreme apprehension. (*Shock 12 hours p.o., dyspnea, empyema*)	Failure of first operation (after its initial success) left her completely defenseless.	17 days Died 17 days p.o.
Case 30 Male: M Age: 36 MS II	Nervous and restless but denies fear or worry. Describes acceptance of "fate" as predicted by doctors.	Pleased that surgeon taking pride in him. Guilty about death of man who failed to survive operation.	Denies fears of crippling invalidism by self-restriction and reliance on authority.	14 days 3 mos. p.o. "Feeling very, very good." "My doctor said I'm not a sick man any more."
Case 31 Female: S Age: 40 MS III	Described former business success but now "four-wall bound." Planned sending body home and hoped for "blessing of a happy death."	Felt "life handed back." Uneasy about former "destructive thinking."	Competitive activity the alternative to guilt and masochistic withdrawal.	Back to work 2 weeks after leaving hospital.
Case 32 Male: M Age: 43 MS IV	Shift from belligerence (toward psychiatrist) to helpless dependence.	Died during operation. (*Difficult hemostatis, cardiac standstill*)	Attempted denial of passivity in preparation for death.	0 days Died during operation.

S: Single
M: Married
W: Widowed

MS: Mitral stenosis
MI: Mitral insufficiency
RHD: Rheumatic heart disease
CHF: Congestive heart failure

AF: Auricular fibrillation
AI: Aortic insufficiency
AS: Aortic stenosis

and operations. The interviews were conducted in a flexible manner and, although some patients were able to respond with a ready flow of associations, others became uneasy unless the psychiatrist volunteered comments and even questions. As one woman (Case 25) put it, "I dry up completely when you sit and look at me like that . . . What kind of thing do you want to know? . . . I wish I could open my mouth and pour."

The psychiatrists were especially alert to the patient's use of words which referred to physiological processes but which could also be symbolic of instinctual drives and emotional attitudes. By using such words as a stimulus it was often possible to obtain further associations from the patient which revealed a great deal about his inner life. One patient (Case 24) described her shortness of breath in terms of choking and suffocation. Further associations led her to mention that she felt smothered. The interview then proceeded as follows:

Patient: . . . Sometimes I'll be smothered—I mean it's just too much attention at times . . . and then I also get very depressed about my condition.

Doctor: You have felt smothered?

Patient: No, I didn't feel smothered with affection. No, I didn't feel smothered. I just felt there were so many—I didn't want anybody to get their feelings hurt. I wouldn't want anybody to get mad . . . I'm sick but there's a lot of people who love me who would like to see me well. Everybody wants to do it in their own way. Mother doesn't want me to do anything. Jim (her husband) says, "You can do it." Mother says, "Don't do it."

Doctor: You feel that they all try to smother you?

Patient: No, not smother me. No, I don't use that word—I feel there's going to be a clash of personalities . . . I feel if they get mad and angry I'm going to get upset.

Doctor: You feel that the effect has been rather smothering?

Patient: Not smothering. I feel that the effect has been overwhelming, and I want to be independent.

In this example the smothering-mothering symbolism is unusually clear, and several of the patients alluded to breathing as a physical shortness of breath but also as symbolic of personal dependence or independence. One patient (Case 8), who had severe episodes of dyspnea, described her completely dependent relationship to her older sister by remarking, "She almost breathed for me." Another patient (Case 5) explained that she could not seem to get her breath in Ohio (where she and her husband lived) but could "breathe better" in Vermont (her mother's home). This patient, who had a very successful operation, later expressed anxiety about the improvement in her breathing: "Taking a deep breath sometimes frightens me. Is it supposed to go way down there?" Another patient (Case 28) described her almost complete dependence upon charity and strangers. She said that she hoped surgery would give her a chance "to do a little breathing on my own." All four of these patients were women, and the breathing seemed to refer to an infantile dependence on the mother or older sister.

Discussions at weekly staff meetings helped to clarify the nature of the patient's use of the interview situation not only to express certain thoughts and feelings but also to strengthen his defenses, for instance, by maneuvering to control the interview or sometimes by behaving in an aggressive way toward the

psychiatrist as a means of allaying his own anxieties. One of the patients (Case 15), for instance, took over the interview politely but firmly, and in her subsequent statements contrasted what she considered to be her brother's abject submission to their mother with her own emotional and economic self-reliance. Another patient (Case 23) remarked, "I didn't know you wanted to know what kind of a person I am—I'm 8C487 in Peter Bent Brigham—this visit to your office is more to me like a business call. I don't like the idea of getting clubby with you really." This kind of behavior demonstrated ego defenses which were characteristic of these patients.

While we were studying the psychological material, we also reviewed the medical and surgical observations in order to obtain an objective picture of what was happening physiologically at the time that we were carrying out our interviews. Follow-up information concerning the patients for six months to a year following their discharge from the hospital was obtained from letters the patients or their physicians had written to Dr. Harken.

MEDICAL AND SURGICAL BACKGROUND

Dr. Harken, the surgeon, and Dr. Dexter, the internist, divided all of the patients in this series into groups based on a clinical classification described in various recent papers[4,5,6] as follows:[5]

GROUP I. This comprises patients whose present course is *benign*. They have auscultatory signs of mitral stenosis, but few, if any, symptoms and minimal evidence of increase in pulmonary vascular pressure. Patients in this group may continue to run a benign course, or they may develop an acceleration of their lesion which shifts them to one of the other groups.

GROUP II includes patients somewhat *handicapped* by a static degree of moderate dyspnea on effort, or by frequent attacks of acute dyspnea, or other pulmonary symptoms usually provoked by an extrinsic cause such as unusual exertion, fatigue, or by infection. Rarely, they may have some peripheral edema but do not have evidence of right ventricular failure.

GROUP III includes patients whose disability is *progressive* rather than static, either with increased dyspnea on effort, or with alarming, increasing, and easily provoked attacks of hemoptysis, chest pain, pulmonary edema, etc. They suffer from palpitation, tachycardia, and distress over the liver on exertion. At any time they may slip into Group IV, or may die of an acute attack of pulmonary edema or from peripheral or pulmonary infarction. Their life expectancy under medical therapy is *hazardous*.

GROUP IV is a *terminal* group. They are completely incapacitated, usually with right ventricular failure, manifested by chronically elevated venous pressure, a considerably enlarged liver, and by a marked tendency to congestion. Their pulmonary disability may or may not be greater than those in Group III. They often have poor liver function, evidence of decreased peripheral blood flow, and many have had emboli. Most of them are in auricular fibrillation.

Most of the patients in the present series had a finger-fracture valvuloplasty.[4] The group includes a number of patients with mitral insufficiency (all in Group IV) in whom an attempt was made to correct the insufficiency by sewing in a lucite ball. As Dr. Harrison Black of the surgical team comments regarding the present study:

The patients undergoing operations for the correction of mitral insufficiency constitute a group which differs in many important respects from those patients who have had correction of mitral stenosis. The latter, unless they are in the Group IV category in which there is considerable

damage to lungs, myocardium and liver, can look forward to a fairly well standardized procedure with low risk (approximately 4 per cent in the Group III patients)* and the expectation of considerable rehabilitation when the stenosis is satisfactorily corrected. The surgery of mitral insufficiency, however, is still in its developmental phases, and the operation carries a much larger risk. These matters have not always been freely discussed with the patients, but they have been by and large aware that their condition differed in many respects from the patients with mitral stenosis. It hardly needs to be added that a frank discussion was always had with the families of all patients.

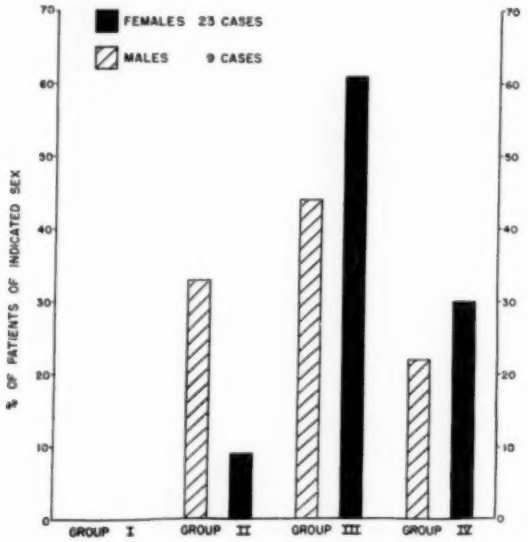


Fig. 1.—Clinical classification of mitral stenosis.

Because of the experimental and developmental nature of the operation for mitral insufficiency at the present time, we have felt justified in offering operation only to those patients who were obviously pre-terminal with a very limited life expectancy. This is true in particular of the four patients in this study who had the operation for mitral insufficiency. The operation itself consists of placing a lucite prosthesis beneath or on the ventricular mitral leaflet. The prosthesis is held in this position by sutures which come out through the ventricular myocardium. We feel that the fatal outcome of these first four patients who were operated on by this procedure was due to the fact that the size and placing of the prosthesis were not adequate; since that time much more encouraging results have been obtained by the appropriate modifications of these features of the procedure.

Five of the patients were in Group II, 18 were in Group III, and 9 in Group IV. The percentage of males and females in the different groups is indicated in Fig. 1.

*Dr. Harken's statistics (personal communication on February 7, 1953) for surgical mortality in these different groups are as follows:

	OPERATIONS	DEATHS
Group I	0	0
Group II	25	1
Group III	280	11
Group IV	170	27

The proportion of 23 females to 9 males is in accord with the sex distribution of mitral stenosis as reported by others and contrasts in this respect to the incidence of coronary disease.[8] The median age for the total group was 37 years (females 37 years, and males 42 years). The number of patients in the various age groups is indicated in Fig. 2.

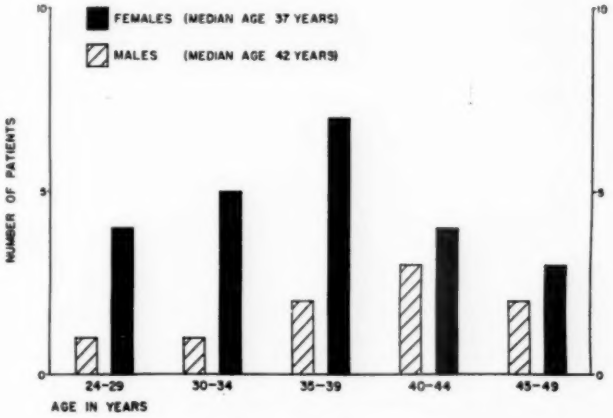


Fig. 2.—Age and sex of patients (median age 37 years).

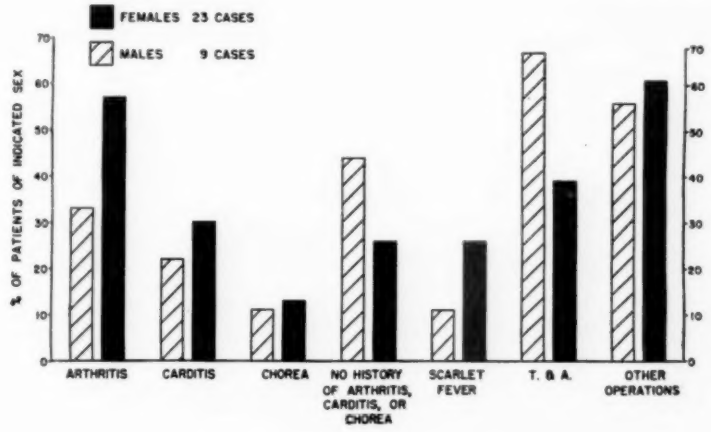


Fig. 3.—Analysis of past history.

Ten of the total of 32 patients gave no history of arthritis, carditis, or chorea Half (16 patients) of the total number remembered an attack of arthritis. The percentage of males and females who gave a history of arthritis, carditis, chorea, or scarlet fever is indicated on Fig. 3, which also indicates the percentage of males and females who had had tonsillectomies and other operations.*

*We are indebted to Dr. Murray Rabinowitz for his help in reviewing the medical records.

PERSONAL RESPONSE TO ILLNESS

The patients in our series had known of the presence of heart disease for an average of 12-13 years (median value for females, 13 years, for males, 11 years). Ten of the patients had learned of their heart disease within the past 10 years, and the other twenty-two had known about it for periods ranging from 10 to 35 years (Fig. 4).

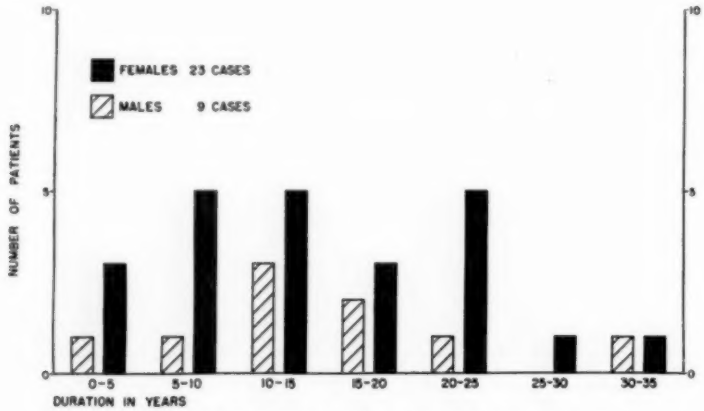


Fig. 4.—Number of years patients knew of heart disease.

The effect on the patient of learning that he had heart disease depended on the stage of his emotional development, his life circumstances, and his personality. One man (Case 1) had tired feelings in his legs when he was 13 years old. He described finding out that he had heart trouble at the age of 14 as follows:

> I was a real active youngster—then suddenly somebody tells you you have trouble with your heart. It never really bothered me so I just didn't slow down . . . I kept on my normal activity like before I found out I had these things . . . I woke up in the middle of the night [a few months later] and vomited. I coughed up blood and bloody sputum . . . It was due to overactivity.
>
> I think my big problem was getting myself to accept the idea that I couldn't do what other people could do. I could never get that through my head. I figured that I was being discriminated against by something—other people could go fishing, play ball to their heart's content. I would have to sit down and watch . . . [It was] a feeling of helplessness—I suppose because there really isn't anything I could do about it. It was there and it limited me . . . I had to accept it. . . . I just didn't accept that I'd really get into trouble. It scared me, too—a kid 14 years old—15 years old to have something like that happen to them. . . . Then [after the hemoptysis] I knew I had to slow down, but it still didn't seem to set just right. I wanted very much to continue with the activity. . . . I suppose it was a mild form of anger at something or other that just slowly became part of me. . . . After that I developed a more or less passive interest in things . . . passive activity.

This boy in his early adolescence was engaged in the struggle to emancipate himself from his family and to establish his masculine identification, and it is not surprising that his psychological response was influenced by these conflicts. He was rebellious and felt that it was a "miscalculation" on the part of his father to expect him to reconcile the whole situation with the kind of religious beliefs his father taught him. His mother, on the other hand, suggested that he learn to play the piano: "You stop and think that up to that time I played baseball,

I played hockey, skating, went fishing, swimming, hunting—all those things." Commenting on his situation, he adds, "I was pretty much on my own. I didn't ever seem to get too much help from the outside." He then tells of having finally found out how to make model airplanes and this was the beginning of his reconciliation to his disease.

Although he felt that his religion later on became the chief source of his strength, he was not able to avail himself of it until he had emerged from his teens. Speaking of the earlier period, he remarks, "I was not much for the church then—after all this talk that they had given me about a God Who cares and so on, I didn't think He would do something like that to me." He says of this, "There was a gradual change with more emphasis being put on the love of God," but this did not come about until some years later when he encountered a minister who, he felt, put a different emphasis on religion than his father had.

When he came for operation he felt "optimistic," feeling that he was living in a "state of grace," and it was evident that he had to a large extent been able to resolve his feelings of rebellion and helplessness by submission to "God's will." The nature of some of the personal problems resulting from the limitation of his activities was indicated during the interview just preceding operation when he asked quite intellectually for statistics concerning the incidence of homosexuality and then established the fact that he had always made it very clear that he was "not interested" in situations where there might have been a sexual approach from homosexuals or prostitutes. Postoperatively he was particularly pleased with the "sharp heart beat instead of (the former) sloppy thud." He got married a year later and reports, "My heart is able to supply the energy needed for the physical aspects of marriage without any noticeable effect."

Seventeen women out of the total number of twenty-three in our series were married, and of these ten had children. Rheumatic heart disease was first diagnosed in five of these women during pregnancy (Cases 5, 8, 18, 24, and 26), which constitutes not only a physiological but also a psychological stress, especially for the woman who has had difficulty in accepting her feminine role. Since motherhood involves an identification with the patient's own mother as well as with her unborn child, the quality of her own psychological progress from girlhood to motherhood becomes especially tested. The discovery at such a time that her heart is diseased and that her future activities may have to be limited can be especially disturbing.

When the discovery of heart disease coincides with a miscarriage or a therapeutic abortion, the woman's psychological attitude may become profoundly altered. One woman (Case 5) became dyspneic during her first pregnancy. Although she was given medical advice to avoid further pregnancies, she had eight miscarriages in the next 13 years, all accompanied by severe dyspnea and sharp limitation of activities. Another woman (Case 24) explained:

"I became ill five years ago for the first time, and then I was very unhappy afterwards. I was pregnant and I had to have a therapeutic abortion. . . . That upset me a great deal and I was very miserable and very unhappy and I didn't seem to do very well after that. . . . I didn't know when I got pregnant that I had anything wrong with me. . . . It came as a complete shock to me. I mean I had never been ill. I've been very active, very athletic. . . . I

used to work and date and run around and have a marvelous time and all of a sudden I find myself become pregnant. I went to a doctor that afternoon. He told me I was over two months pregnant. . . . That night I went home and had a terrific attack of pulmonary edema, was rushed to the hospital, and almost three weeks later I had a therapeutic abortion. Well, I mean that was a complete change in my life altogether . . . I felt like if I didn't have that baby I would never have any. . . . Now Dr. Harken says, "Do you want to have a baby?" and I says, "Of course." Well, I want to have a baby because I feel that is a part of having a normal family, but I mean, so much happened the first time in having a baby—as much as I'd like to have one, I sometimes wonder if I really want one now. Is that abnormal?"

KNOWLEDGE OF HEART DISEASE AND AWARENESS OF DYSPNEA

The patient's awareness of shortness of breath did not necessarily coincide with finding out that he had heart disease. Some patients knew of their heart disease for many years before they first became aware that they had difficulty in breathing. Others were conscious of dyspnea for quite some time before heart disease was diagnosed. The awareness of dyspnea may be a realistic response to the increasing disturbance of the cardiovascular function, but the time when the patient becomes conscious of his shortness of breath may be determined by experiences to which he is psychologically vulnerable. The patient quoted above (Case 24) had her first attack of pulmonary edema the day she learned that she was pregnant. One of the men (Case 4) first had shortness of breath shortly after he had been rejected by the draft board, and another man (Case 7) first became aware of dyspnea after he had been hospitalized for minor shrapnel wounds.

ATTITUDE TOWARD LIMITATION OF ACTIVITIES

The attitude of the patient toward limitation of activity was influenced by the meaning of the illness to him. One woman (Case 8) described her experiences as follows:

"It was hard to get used to walking to a bus when I had been in the habit of running. . . . I just felt extremely defiant . . . but I tended to live as I had always lived and yet I was very repentant when I'd be taken with a spell. I'd know that I had done things that I shouldn't have done or I wouldn't have been where I was, but at the same time I couldn't stop myself . . . I wouldn't give in to it . . . I would purposely let myself get worse and worse . . . I didn't want to become a hypochondriac. I didn't want to become one of those persons that thought every time I had a pain in my finger, well, it was directly connected with my heart, and that's what I more or less was afraid would happen to me. . . . I can't see why anyone would want to bring illness onto themselves if they didn't actually have it, although I did do one thing when I was a child that I'll never forgive myself for . . . I told them I had heart trouble at that time (aged 8), and I actually had myself almost believing it. For no reason whatsoever than I wanted to make up a good story—just to pull a little attention to myself, I guess, more than anything else. . . . When I discovered I really did have it [at the age of 23], I thought back to the time when I had told that so many times. . . . It was a deliberate falsehood. . . . Maybe I was getting my just deserts for doing it . . . because I have heart trouble now . . . I wonder if I did bring it on myself by telling it."

Her defiance of activity limitation and purposely letting herself get worse represent her masochistic need for punishment and her attempt to defend herself against this urge. Another patient (Case 30) explained that he was told by the

school doctor that he had mitral stenosis when he was trying to get on a team at the age of 15. He restricted himself severely thereafter. "I kept pretty well within boundaries." He describes his regimen as "clean living" and it was evident that his physical self-limitation coincided with a more general moral restriction. This patient was guilty and uneasy about his competitive and aggressive urges, remarking:

"I'm the kind of a fellow that gets excited very easy . . . I have to blow my top—if it comes to a point of real hot discussion, I seem to get all heated up. . . . When we were kids if somebody wanted to start a fight or an argument, I didn't think twice. If he wanted to fight, he'd get it . . . I was very very high strung and then after it was all over I'd feel a little shaky and cool off. . . . I began to get tensed up and build up a tension inside and if you don't know how to handle me, it probably will come to a point where I would take a shot at you or something like that."

In contrast to the woman who felt so rebellious, this man repressed his aggression and was good and obedient.

LONG-TERM DEFENSES

Review of the histories had resulted in the recognition of three leading types of psychological defenses upon which the patients have relied to counteract the threatening implications of the advancing disability and disease. These relatively long-term defenses included *narcissism* in various forms, *submission* to a higher power (God, "fate," or the doctors), and *activity*. In the men these defenses were resorted to in order to counteract the threat to masculine integrity because of the crippling and disabling nature of the illness. Most of the men apparently depended on the first two of these defenses, although many of them also stressed their interest in activity as part of their concept of their own manhood.

In at least ten of the women patients (Cases 2, 3, 8, 14, 15, 18, 21, 22, 24, and 31), activity in one form or another had been very much emphasized. Dunbar[3] has described patients with rheumatic heart disease as ambitious in a vague way, inclined to overdo, and with an interest in athletics which led them to overtax themselves. In a number of our women patients, the emphasis on activity seemed to serve as a defense against the fears of infantile regression to a masochistic dependence on the mother. Although the extent of the woman's reliance on activity as a defense became clearly manifest when it was threatened by the progress of the disease, there was clear-cut evidence in a number of instances that an active urge to compete with men had been an important characteristic previous to the onset of rheumatic heart disease.

One woman (Case 31) dwelt extensively on her former activities as a business executive. She had tended to ignore her symptoms and kept on swimming and climbing stairs until five years before admission to the hospital, when she developed pneumonia and became severely decompensated. This collapse immediately followed the resignation of her business position after a male superior had, as she put it, "tried to break my will." She described her subsequent limited existence as "four-wall bound." It developed that she had made plans to have her body sent home in case she did not pull through the operation, so her mother would not have to make the trip. She had brought along a crucifix which had belonged to another person who experienced the

"blessing of a happy death." Her operation was very successful, but she became uneasy about interviews postoperatively, felt she was being "tested" and that perhaps there was something wrong with her mentally. She felt that she had been on the verge of "destructive thinking" and this apparently represented some concern about her aggressive feelings. She now felt as if "somebody has handed my life back." It was characteristic of her that she was at work two weeks after leaving the hospital.

Three of the men (Cases 1, 10, and 30) had attempted to resolve conflicts concerning aggression and passivity by submission to a higher power. All three patients made use of their religion in this way. The man (Case 1) who came to the operation in what he felt to be "a state of grace" has been described. As he put it, "I'm quite optimistic. If it doesn't work out, well, I feel I'll be in a better place than I am here now. . . . God will give you whatever He feels is right." The man who severely limited himself both morally and physically (Case 30) admitted that he was nervous and restless but denied any fear. "Knowing I have a condition that was serious, I just followed instructions. . . . I positively keep worry out of my mind—I'm just not the worrying kind." He told of not worrying even when he coughed up blood because doctors had warned him that his heart would "kick up" at 35 (he was now 36) and that "I would probably become an invalid or a cripple. . . . I figured the time had come." He described his belief in a supreme being—"When He wants you, He'll call you." A third (Case 10) remarked preoperatively, "The Almighty is calling me. . . . I put myself in His hands altogether, so whichever way it goes I feel it's for the best."

A narcissistic type of defense was apparently important to four of the patients (Cases 4, 7, 9, and 15). One was a woman (Case 15) who was rather seductive, dressed glamorously, and spoke of what good care she had taken of her body, in an apparent attempt to assure herself that she would get through the operation without bodily harm. One of the men (Case 4) talked in a blustering way and displayed his big muscles. Although his operation was technically successful, the invasion of his body constituted a psychological threat to which he reacted with anxious hypochondriasis and a good deal of querulous complaining about various bodily discomforts. Another man (Case 7) emphasized his unusually good health before the discovery of rheumatic heart disease and told quite directly of the unusual importance physical and athletic prowess had for him. "I went to college to become a football coach. It's the only thing I ever wanted to be as long as I can remember. I never changed my mind the way most kids do." He denied any fear, which he apparently thought of as a betrayal of weakness.

EMERGENCY DEFENSES

Immobilization.—This last patient's course illustrates the way in which the progress of the disease may undermine a leading personality defense (in this case body narcissism) so that the patient is forced to rely on emergency defenses which tend to be more primitive. At the time this patient was admitted to the hospital he had become immobilized and almost like a statue. He was silent and expressionless and gave answers to questions with impassive obedience. Five days

after the operation he showed the same taciturn immobile behavior and was obviously uneasy about having to lie in a supine position, insisting on sitting up. A month after operation he reported somberly that he was feeling "marvelous," adding, "getting away from those needles is a help." He attributed his weakness to body changes—weight loss and the salt-free diet. The emergency defense in this patient was immobilization as a final denial of weakness.

Another patient illustrates the resort to immobilization and also to amnesia as defenses against probable fears of disintegration.

A woman (Case 11) was frozen and expressionless. She spoke barely audibly in a monotone with long pauses and made no spontaneous comments. She had adjusted to her cardiac disability by doing less, moving less, and talking less, and finally was unable to raise her voice above a whisper. After the operation she spoke with greatly increased expression but still told very little about herself. "I don't know what to say." She remembered nothing from the night before the operation until three days after it. Severely stressful experiences in her background included a pregnancy at the age of 31 (she was now 33) in spite of medical advice to the contrary which had then been interruped by therapeutic abortion in the third month.

Hysterical Amnesia.—Hysterical amnesia or depersonalization constituted emergency defenses in four of the patients (Cases 8, 10, 11, and 20).

The long-term defenses of the woman (Case 8) who felt so guilty about having pretended that she had heart disease as a child have been described. She became very frightened at the imminent approach of the operation and the day before remarked, "I feel a little numb in a way—just as though I'm kind of sitting apart and watching it go on more or less. . . . It's almost unbelievable, as though it isn't really happening, more like a dream. . . . It doesn't seem real that it's happening. . . . It's kind of like looking at it through a haze." During the first and second postoperative days the surgical house officer described her as lying with her eyes open but as though she were blind and she did not seem to be at all sensitive to pain over her left chest. On the third postoperative day there was a sudden output of 5 liters of urine, and it was found that she had a very low blood sodium.

A few days later she herself described what happened as follows: "They said I went balmy and I did. I just couldn't make heads nor tails of anything. . . . I felt numb. . . . Everything was like sitting back and watching things on a screen. . . . The nurses' movements were mechanical. I said, Nurse, are you a real woman? . . . I didn't know what they had done to me—it's almost as though I was dead and watching them."

An hysterical kind of depersonalization and unreality were evidently emergency defenses against frightening phantasies about the operation in this patient who had felt so guilty about her disease. Although this response became much more accentuated postoperatively until after the diuresis on the third day, the psychological pattern had already been clearly established during the last interview previous to her operation.

Belligerence, Excitement, and Denial.—Other emergency defenses included belligerence, excitement and desperate denial. The belligerence in two of the men represented a final protest against their own passive wishes.

One (Case 32) was at first very belligerent toward the psychiatrist, asking "What are you poking your nose in my business for?" After two interviews and after he had canceled six, there was a complete reversal in his attitude. He became confiding and confessed his feelings of weakness. He was ashamed of not wanting to know the date of the operation instead of "walking up to it and taking a smack at it." Just before the operation he pleaded laughingly with the psychiatrist, "Don't coax me. Don't take advantage of me when I'm helpless."

In the face of death this man was able to use his relationship to the psychiatrist to make a more comfortable compromise with his unacceptable urges to yield and surrender.

The other man (Case 20) was outwardly calm and cooperative but expressed suspicion of the psychiatrist's motives. He denied that he was brooding about his disease. He wanted explanations of the operation but stated, "I know about all there is to know about the operation. It's like a plumber—the damned old pipe is plugged up with scale and it has to be scraped or cleaned out." He was 36 years old and planned on marriage if the operation was successful. Postoperatively visual impairment developed which was diagnosed as resulting from occipital lobe ischemia. The degree of visual impairment was highly variable and an hysterical factor was suspected. He was one of the four patients who was unable to remember anything of the first 3 postoperative days. He became very resentful and openly hostile toward the psychiatrist, remarking angrily, "You're not doing me any good."

This patient's belligerence as well as his postoperative amnesia were evidently defenses against the possible development of a paranoid panic and it may have been that his visual impairment was hysterically exaggerated because his concern about his eyes or his eyesight referred to unconscious sexual fears.

Two of the women became excited (preoperatively and the other also preoperatively but to a much greater extent after the operation was over).

One (Case 26) was very much excited preoperatively. She cried, occasionally yelled and banged on her pillow. With the increasing limitation of her activities during the past few years, she had developed a variety of paralyses and other hysterical symptoms. She expected the psychiatric interview to be a pelvic examination, gave a highly emotional account of certain sexual experiences, and seemed relieved thereafter. She phantasied the surgeon as "Svengali-like" and did not want to know the date of operation. Postoperatively she described "seeing" the psychiatrist in the operating room and feeling comforted because he would not let her be hurt. She asked insistently if the psychiatrist had really been there and cried and complained of pain when her phantasy was not confirmed. Subsequently she cheered up and actively encouraged the other patients around her. Five months postoperatively she was reported as making excellent progress with no further hysterical symptoms or evidences of excitement.

This woman's hysterical excitement reached its height just before the operation. Her sexualization of her relationship to the psychiatrist served as a defense against her terrifying phantasies about the surgeon and the surgical procedure.

Another (Case 5) was very talkative preoperatively. She had begun to be somewhat excited when she found out that she was "an acceptable candidate for surgery." She described having had "a beautiful dinner" after getting this decision from the surgeon. Postoperatively she became much more excited and very active. She spoke of "an uncontrollable surge of energy." On the seventh postoperative day she remarked, "I feel strong enough to carry you pickaback. I can now do all the things I have been wanting to do all my life." It was only 15 months postoperatively that her elation began to subside and its function as a denial of pain which by now had probably become a depressive equivalent became quite evident. She was still talking incessantly but remarked, "I get that pain. It's so constant and I've been more or less kind of ashamed of myself to complain about it. . . . It's getting to the point now where even trying to convince myself that I'm up on the pink cloud don't make so much of an impression."

At least one of the patients in this series resorted to the emergency defense of desperate denial.

A 45-year-old married woman (Case 17) looked chronically ill and wasted. She remarked, "I can't handle my fluids. It's very distressing and painful. My liver enlarges, it causes me so

much pain. I get short-winded and gasp and gasp." In spite of her desperate physical state, she managed to deny her fears by an apparently untroubled confidence in the outcome of the operation. "It's been a 96 per cent success I've heard."

FAILURE OF DEFENSES

In some instances the stress was so severe that the patients seemed to be virtually defenseless and were close to panic.

One woman (Case 13) became so frightened at the prospect of the operation that she asked her husband to take her home. She insistently expressed the fear that her heart might stop beating during the operation, adding, "I'd just be dead. I have everything in the world to live for. I want to live and if I want to I know I will." She was the only patient in the series who expressed a fear that her heart might stop beating, and she was the only one who had an operative cardiac standstill lasting almost 10 minutes. She made a good recovery and was "very elated and very grateful. . . . I didn't think a person could live with their heart stopping for 10 minutes, but I did. . . . It's like a dream and I just don't want to think about it any more. . . . I feel like a different woman." Five months postoperatively she expressed gratitude to the surgeon "for giving me this new life."

Another woman (Case 14), who died 21 hours after the operation, was terrified beforehand that she would not survive. She talked incessantly, alternately laughed and cried, and could not sit still. "I'm scared. . . . I'm afraid I won't live."

DEFENSES "CHRONICALLY DECOMPENSATED"

In a few instances the psychological defenses were inadequate and unsuccessful to such an extent that the patients bordered on psychosis, a situation which might be described as "chronic psychological decompensation," and this greatly hindered their convalescence.

CASE 28. A 39-year-old divorced woman, described her almost complete dependence upon charity and strangers. Her mother had died of cancer 18 months previously and her only daughter had recently married. She threatened to hang herself in the hospital bathroom if surgery was withheld. After operation she confessed stealing salt and eating large amounts of it. She complained of intense pain and felt if she had to face operation again she might not go through with it. She died two or three weeks after leaving the hospital.

CASE 16. A 37-year-old widow, received increasing amounts of analgesic drugs following the onset of left chest pain five years ago. She had a cardiac sympathectomy three years ago and was bitterly critical of the surgeon when mitral surgery was recommended a year later, insisting that she had been misinformed concerning the nature of her first operation. Shortly after sympathectomy, she was in a mental hospital for three weeks because of a psychosis due to barbiturates. After a successful valvuloplasty, she was at first delighted but in the succeeding weeks and months became aggressively demanding toward her surgeon and at the same time tried to dissuade the patients in his waiting room from undergoing surgery. Fifteen months postoperatively she was still on narcotic drugs because of pain.

CASE 18. A 34-year-old mother of three children who had been separated from her husband, described her "amused bitterness" about her disappointed ambitions. "When I was younger I always used to say, 'I'm not going to get married'—I was just very much interested in a career . . . and I never liked children . . . I had to take care of my sister (who died)—I had enough children before I was grown up." She felt guilty about the deaths of her stepfather and her fiancé, having quarreled with each of them just prior to their deaths. "I couldn't afford to study and I had a throat operation. . . . That's when they discovered I had heart disease. From then on it was rather a frustrating affair . . . when I'd always been so active to have everything completely turned around. . . . I guess I didn't care what happened—that's why I got married. I mean, I had no interest in anything or anybody." She mentioned an attack of cardiac failure six months before admission: "I began to be a little afraid that I wouldn't come out of it."

She commented on her imminent operation. "You contact death with ether . . . with a heart condition." She added, "I suppose all heart attacks are brought on by people themselves." After the operation she complained of persistent pain, "I just don't want to eat. I can't seem to concentrate. Sometimes you can't see very good. . . the only thing you know is pain." Four months postoperatively she reported, "If you want my honest opinion, it isn't worth it . . . I get very tired." She was reoperated but did not improve, and she remarked, "There's no incentive. I try not to be resentful." Six months postoperatively she was readmitted for the third time complaining of incisional pain. Sizeable amounts of narcotics and several intercostal and incisional blocks brought only moderate relief. Nine months postoperatively she is reported to have been admitted to another hospital for treatment of recurrent rheumatic activity.

The persistence of pain in this patient does not seem to be entirely accounted for by her disease or by her physical response to the operative procedure. She associated pain with being hurt and described her reaction to getting a letter from her husband's lawyer, stating that her husband did not have to support her: "For a minute I would like to have gotten him by the neck. . . . I think I was a little bit angry. . . . . I was not heartbroken." Speaking of her relationship to her mother during her earlier life, she continued, "I didn't always accept things as easily as I do now. . . . There were times when I would like to get very mad. . . . I try to bury all those things. . . . I suddenly realized one day that nobody could upset me or hurt me unless I let them. . . . I find that things amuse me now that didn't before."

It seems fairly evident that this woman's active strivings for a career represented her struggle against the masochistic resignation with which she responded to the accumulation of personal disappointments as well as the increasing limitation of her activities brought about by the advance of her disease process. Although there may have been an organic explanation for her pain, from a psychological point of view it seems to stand for resentment, guilt, and depression. The nature of her fears about anesthesia suggests that she may have had rather strong death wishes. As Helene Deutsch says, "Going to sleep under the narcosis often represents the realization not only of the fear of death but also of the wish for death." This patient had quarreled bitterly with her mother during her girlhood and the relationship was still a very difficult one at the present time. As Deutsch remarks, "The increased tie to the mother (which develops under the pressure of anxiety and the burden of the feeling of guilt) can receive a new regressive thrust in the moment of the danger from an operation. The masochistic turning of the aggression against the person's own ego then brings about the ominous state of clinging to the suffering and to the postoperative symptoms."

In all three of the above patients it was quite clear that the psychological "decompensation" had been established long before the patient came for operation. The patient (Case 5) described earlier, who developed a definite hypomania which only began to subside 15 months postoperatively, should also be considered with this group. In her case, it became quite evident that both elation and overactivity served to deny her underlying feelings of depression, which as in these three patients was expressed as pain. In two cases (Case 28, the woman who threatened to hang herself in the hospital bathroom preoperatively, and Case 16, the woman who had a previous psychotic episode), it could be predicted that there would probably be considerable psychological disturbance after the

operation. We did not have this conviction about the third patient (Case 18), although with the advantage of hindsight it now seems quite understandable that she should have reacted as she did. The woman who became hypomanic (Case 5) was already somewhat excited preoperatively, and probably this should have warned us of what was likely to follow, although we did not actually foresee the extent of her hypomanic development.

TRANSFERENCE TO SURGEON

Nine of the patients with successful operations (Cases 2, 5, 8, 9, 13, 24, 25, 27, and 31) were elated or euphoric. Most of these patients were joyful and expressed their loving gratitude to the surgeon. Three of the patients (Cases 12, 23, and 24) said they felt reborn or that they had been given new life. One woman (Case 31) felt that her life had been "handed back." Another (Case 2) reported, "I feel marvelous . . . I told [the surgeon] 'You're the man I love for giving me back my health . . . I feel I can start my life all over again.'" Two of the patients (Cases 8 and 25) described the operation as "a miracle." Some of these statements gave an indication of the nature of the transference to the surgeon as well as the meaning of the operation to the patients.

One rather slender man (Case 27) who was only 5 feet 2 inches tall, had been married to a 6-foot woman who weighed 235 pounds, and he "seemed to fall apart," as he expressed it, after her death. Following the operation he was bubbling over with enthusiasm and felt "reborn" but continued to be extremely dependent on his younger brother—"I have come to depend on him the same as I did my wife." A few months after he left the hospital, he remarried. He sent the surgeon a greeting card on Mother's Day signed "Your reborn son."

At least one of the patients, however (Case 26), phantasied the surgeon as a sadistic attacker—"Svengali-like." Although for some (Case 8) he seems to have been thought of as a divinely guided father figure, for others (Case 21), he seems to have been regarded more as an undifferentiated protective parent (essentially a mother). One of the women patients (Case 18) apparently saw the surgeon as the personification of her own active strivings: "He reminds me of the way I used to be. I was never still. I was very active. He amuses me." A little later she "wondered" what would happen if he should have a heart attack. The same patient apparently saw the psychiatrist, on the other hand, as the embodiment of her present passive resignation, commenting that he looked "tired" and as though he felt resigned.

TREATMENT

By far the most important psychotherapeutic influence was, of course, the successful outcome of the operation, which in so many instances quite literally rescued the patient from imminent death and restored him to life and hope; the elated feeling of many of the patients was an understandable response. It seems likely that for some of them the narrow escape from death also signified atonement for past guilt as well as rescue from crippling disability and the removal of the threat of separation from friends and family. In contrast to other operations, these patients were not deprived of any part of the body and could easily

feel that they had been given something new and wonderful instead of having something taken away.[9] As one patient (Case 22) phrased it, "I feel as though you had given me a brand new heart."

These patients were delighted to show themselves to new candidates for the operation and helped to create an atmosphere of hopeful expectation. This high morale was helpful most of the time but created additional difficulties for some of the patients who did not do well postoperatively. One woman (Case 19) became tearful and expressed the feeling that the surgeon was disappointed in her and that he had expected her to be up and around like the others. She also fel that the nurses did not know about her case and were asking her to undertak activities that were too much for her. She died of congestive heart failure 45 days after her operation. One of the patients who did very well (Case 30) was pleased that the surgeon seemed to be taking so much pride in him but felt very guilty when a fellow patient failed to survive the operation.

Quite a number of the patients were much reassured by the careful explanations they had received from the internist concerning the different tests that were being carried out, and they trusted his clear evaluation of their physiological status. The surgeon allowed the patient to choose whether or not he wanted to know the exact date of operation ahead of time. This allowed the patient to make use of his characteristic way of dealing with such situations. Some felt a reassuring sense of control when they possessed intellectual knowledge of what was ahead and others with a strong need for denial preferred the protection of ignorance.

The psychiatric interviews turned out to be very helpful to many of the patients. They provided the opportunity for an expression of anxious feelings and frightening thoughts which the patient was better able to manage after talking them over. A number of the patients immediately established a surprisingly intense relationship to the psychiatrist and were able in some instances to make use of this as a means of mitigating fears and phantasies about what might happen during the operation.

DISCUSSION

In order to keep a true perspective it has been necessary throughout this study to examine the psychological responses of the patients against the background of their physiological upheavals. The attempt to take full account of each patient's life history and his characteristic way of reacting to his difficulties has made it possible to clarify many of the clinical manifestations in terms of an interaction of the physiological and the psychological forces. The fact that these patients were under such severe stress at the time that we observed them provided an unusually favorable opportunity for catching a glimpse of some of their major psychological conflicts in a very short time. Although we were able to observe some of the more outstanding reactions in each patient, the brevity of our contact did not make it possible to establish that dependable grasp of the biographical development which can only result from careful and relatively prolonged study under much more favorable conditions. We did not even attempt to evaluate the significance of the childhood history,[7] and it was not possible to

establish the relative strength of the instinctual trends whose manifestations we were able to observe. In some instances we saw only the emergency defenses and have very little indication of what the patients had been like during less stressful periods of their lives.

We were somewhat surprised to find that we did not encounter the hysterical phantasies about the heart as a sexual organ which are so familiar in the treatment of patients with anxiety hysteria. All of these patients reacted to the cardiac operation in terms of death or survival and the heart symbolized the life of the whole person.

Our preoperative study of the patient's response through the years to limitation of his activity and our observation of his spontaneous use of the preoperative interviews gave insight concerning the nature of his psychological defenses. In most cases it did not enable us to make accurate predictions concerning the patient's postoperative course, partly because of the brevity of our observation but also because there were too many psychological variables and the organic factors were, of course, beyond psychological control. The development of unexpected postoperative complications, for instance, sometimes brought out anxieties in patients who had shown no disturbance preoperatively or postoperatively up to that time (Case 3).

In some instances these interviews were helpful in evaluating the severity of the organic disability by showing that the patient had a special attitude toward his symptoms which influenced his awareness of them (Case 20).

Six of the patients in the present series had obvious emotional disturbances following the operation (Cases 3, 5, 12, 16, 19, and 28). Emergency treatment in this series of patients, all of whom had been seen preoperatively, was found to be more effective than was often the case in other patients, where there had not been any opportunity to establish a preoperative relationship and thus to gain a better understanding of the patient's personal problems.

SUMMARY

1. Thirty-two patients with mitral stenosis who had mitral surgery were interviewed by psychiatrists preoperatively and also postoperatively. An understanding of long-term adaptation to progressive limitation of activities provided the necessary background for the recognition of emergency defenses as they developed in the hospital situation both before and after operation.

2. The interviewing technique focused on emotionally meaningful material concerning the adjustment to limitation of activities and on the feelings and phantasies about the operation. Complete tape recordings were made of all the interviews. This information was then condensed to the essential preoperative and postoperative observations and charted with a brief interpretation of the psychological defenses illustrated by each case. The most important medical and surgical events during hospitalization were also reviewed and charted.

3. The patients were grouped according to the clinical classification of Harken and Dexter as follows: Group I, 0; Group II, 5; Group III, 18; Group IV, 9 (in 4 of these, mitral insufficiency rather than mitral stenosis was predomi-

nant). There were 23 females and 9 males. The median age was 37 years. The medical histories were summarized and charted.

4. The effect on the patient of learning that he had heart disease depended on the stage of his emotional development, his life circumstances, and his personality.

5. The awareness of dyspnea was found to be a realistic response to the increasing disturbance of the cardiovascular function but was also influenced by experiences to which the patient was psychologically vulnerable.

6. The attitude of the patients toward limitation of activity was influenced by the meaning of the illness to them.

7. Long-term psychological defenses included narcissism, submission to a higher power, and activity. Emergency defenses included immobilization, hysterical amnesia or depersonalization, belligerence, excitement, and desperate denial.

8. In some instances the stress was so severe that the patients seemed virtually defenseless and were close to panic.

9. In others the psychological defenses were inadequate and unsuccessful to such an extent that the patients bordered on psychosis. All of these complained of pain to such an exaggerated extent that it seemed to represent a masochistic clinging to suffering.

10. The transference to the surgeon is described and psychotherapy is discussed.

REFERENCES

1. Deutsch, F.: Applied Psychoanalysis, New York, 1950, Grune & Stratton.
2. Deutsch, Hélene: Some Psychoanalytic Observations in Surgery, Psychosom. Med. **4**:105, 1942.
3. Dunbar, Flanders: Psychosomatic Diagnosis, New York, 1948, Paul B. Hoeber, Inc., pp. 367-434.
4. Harken, D. E., Dexter, L., Ellis, L. B., Farrand, R. E., and Dickson, J. F., III: The Surgery of Mitral Stenosis: III. Finger-fracture Valvuloplasty, Ann. Surg. **134**:722, 1951.
5. Harken, D. E., Dickson, J. F., III, and Ottosen, P.: Surgical Correction of Mitral Stenosis, M. Times, New York, November, 1952.
6. Harken, D. E., Ellis, L. B., Dexter, L., Farrand, R. E., and Dickson, J. F., III: The Responsibility of the Physician in the Selection of Patients With Mitral Stenosis for Surgical Treatment, Circulation **5**:349, 1952.
7. Jessner, Lucie, Blom, G. E., and Waldfogel, S.: Emotional Implications of Tonsillectomy and Adenoidectomy on Children, Psychoanalytic Study of the Child **7**:126, 1952.
8. Levine, S. A.: Personal communication.
9. Lindemann, E.: Observations on Psychiatric Sequelae to Surgical Operations in Women, Am. J. Psychiat. **98**:132, 1941.

PATHOLOGIC PHYSIOLOGY AND DIAGNOSTIC SIGNIFICANCE OF THE PRESSURE PULSE TRACINGS IN THE HEART IN PATIENTS WITH CONSTRICTIVE PERICARDITIS AND PERICARDIAL EFFUSION

RUSSELL H. WILSON, M.D., PH.D.,* WAYNE HOSETH, M.D.,**
CHARLES SADOFF, M.D.,** AND MARY E. DEMPSEY, M.S.**

DALLAS, TEX.

THE diagnosis of pericardial disease is often difficult because of similarity of the signs and symptoms to noncardiac disease and cardiac disease of other origin. The signs and symptoms associated with constrictive pericarditis are dyspnea, venous distention, edema, serous effusion, small pulse pressure, and pain in the chest. These physical signs and historical data are associated with other forms of cardiac and pulmonary diseases and do not serve as differential points in the diagnosis of pericardial disease. The electrocardiogram and roentgenogram likewise do not give exclusive information.

Right-heart catheterization has made feasible the measurement of the pressure of the blood in the brachial veins, superior vena cava, right atrium and ventricle, the pulmonary artery, and the pulmonary veins[1] in patients with pericardial disease. Evaluation of older physiologic concepts of pericarditis is now possible.

The physiologic criteria of pericardial disease determined by right-heart catheterization have been considered to be: first, an M or W contour of the pressure tracings of the right atrium; second, an early diastolic dip followed by a rapid rise of right-ventricular diastolic pressure to form a plateau[2-5]; third, a ratio of the right-ventricular end-diastolic to systolic pressure greater than one-third[6]; and fourth, a great decrease in the pressure difference between the right atrium and pulmonary artery.

Although these physiologic values are characteristic, they are not specific for pericardial disease since they have been found in right-heart failure in other forms of cardiac disease.

The purpose of this study was to determine the reliability of these criteria in the differentiation of pericardial disease from other forms of cardiac disease with failure of the right side of the heart.

Received for publication April 12, 1954.

*Department of Medicine, Southwestern Medical College of the University of Texas and the Veterans Administration Hospital, McKinney, Tex.

**Veterans Administration Hospital, Minneapolis, Minn., and the Medical School of the University of Minnesota, Minneapolis, Minn.

TABLE I. RIGHT HEART CATHETERIZATION DATA FROM 10 PATIENTS WITH CONSTRICTIVE PERICARDITIS AND 3 PATIENTS WITH PERICARDIAL EFFUSION

	AGE	CARDIAC INDEX	OXYGEN SATURATION HGB. %	MEAN SUPERIOR VENA CAVA PRESSURE (MM. HG)	MEAN RIGHT-ATRIAL PRESSURE (MM. HG)	DIP	RIGHT VENTRICULAR PRESSURE (MM. HG)	RIGHT VENTRICULAR RATIO D/S (%)	PULMONARY ARTERIAL PRESSURE (MM. HG)	DIFFERENCE BETWEEN RIGHT-ATRIAL MEAN AND PULMONARY ARTERIAL DIASTOLIC PRESSURES (MM. HG)	PULMONARY ARTERIAL WEDGE PRESSURE (MM. HG)	BLOOD PRESSURE (MM. HG)	DATE OF SURGERY	DATE OF RIGHT HEART CATHETERIZATION	REMARKS
Chronic Constriction															
1. F.I.*	25	2.47	93	19	19	+	35/19	54	35/19	0	—	105/75	6- 2-47	8- 8-47	
*	30	4.57	98	10	9	+	30/9	30	30/9	0	10	95/70		10-15-52	
2. M.M.	35	2.26	91	16	16	+	34/16	47	34/16	0	—	128/82		3- 1-52	
*	38	1.52	99	6	6	+	29/6	21	29/10	4	10	140/90	6-22-53	8-27-53	
3. J.G.	29	1.93	94	18	17	+	32/17	53	32/17	0	—	105/80	10-26-53	7-13-50	
	32	3.40	96	22	22	+	39/22	56	39/24	2	21	110/80		7-15-53	
4. A.O.	57	1.18	94	17	16	+	36/16	44	36/17	1	—	136/82	12- 8-50	11-10-50	Died at surgery
5. C.MacG.	34	1.83	97	19	19	+	40/19	47	40/20	1	—	100/85		1-21-52	No surgery
6. R.W.	34	2.93	91	22	22	+	39/22	56	39/24	2	—	125/95		9-15-52	No surgery
7. J.J.	42	2.80	89	18	18	+	44/18	41	44/23	5	—	110/100		8-12-52	No surgery
8. R.B.	50	1.86	97	19	18	+	31/18	58	31/18	0	18	120/80	8- 3-53	5-22-53	
9. S.G.	60	3.26	93	18	18	+	37/18	51	37/19	1	—	110/80	4-16-53	4-14-53	
10. E.F.	57	2.63	91	15	15	+	38/15	50	38/15	0	15	136/76		11-12-53	No surgery
Acute Effusion															
11. C.M.	58	2.31	97	8	8	+	20/8	40	20/11	3	—	184/110		5-16-50	Autopsy
12. E.M.	25	1.87	93	19	18	0	39/15	38	39/23	5	—	124/80		5-25-50	Pericardial tap 4-14-48
13. J.H.	41	2.24	92	23	23	+	28/17	61	28/25	2	25	137/107		11-10-53	
†	41			8	8	+	19/6	32	19/12	4	6	130/90		11-10-53	Pericardial tap 11-10-53
Mean value for 14 normal persons	34	4.1	98	3	3	0	20/3	15	20/9	6	4	120/70		—	
Mean value for pericardial disease	42	2.28	93.2	17.5	17.5		34.8/16.8	48.0	34.8/19.0	2					

*Following surgery †Following pericardial tap

METHOD

Ten patients with chronic constrictive pericarditis and three with acute pericarditis with effusion and tamponade were studied. A catheter was inserted into the superior vena cava and through the right atrium, ventricle, pulmonary artery, and then wedged when possible into a small pulmonary artery for measurement of pressure sequentially.[7,8] Pressures were recorded with a 15 lb.-Statham pressure transducer and a Sanborn four-channel direct-writing recorder. The pressure-measuring reference point used, assumed to be at the level of the right atrium, was 10 cm. above the skin of the back.[9] The pressure transducers were calibrated with a mercury manometer.

The blood gases were determined by the method of Van Slyke and Neill.[10] The cardiac output was determined by the direct Fick principle.[11] The oxygen uptake was measured by the method of Haldane.[12] Femoral arterial blood samples were collected anaerobically as outlined by Wilson.[13] In a series of twenty-four normal persons the range of the right-ventricular diastolic pressure never exceeded 5 mm. Hg. The criteria for right-heart failure were right-ventricular diastolic pressure equal to or more than 5 mm. Hg and clinical signs of failure such as venous pressure of the same magnitude, prolonged circulation time, enlarged liver, distended neck veins, ankle edema, and serous effusion. The end-diastolic pressure was used to calculate the ratio of the right-ventricular diastolic to systolic pressures.

The data obtained from these cases were compared to data derived from the catheterization studies of 453 cases of cardiac disease of diverse etiology.

RESULTS

The data in Table I are from ten patients with chronic constrictive pericarditis and three patients with acute pericardial effusion. The mean normal values were collected from fourteen normal adult persons.

The cardiac indices were unformly diminished in all patients with pericardial disease. The stroke output was below the mean normal level. The mean arterial oxygen saturation was 95 per cent, which is below the value of 98 per cent for the fourteen normal persons. The right-atrial mean pressure ranged from 6 to 23, and the average was 18 mm. Hg. The pressure in the superior vena cava was equal to that in the right atrium. The systolic pressure in the right ventricle was elevated, the range was 28 to 40, and the average was 35 mm. Hg. The diastolic pressure range in the right ventricle was 6 to 22, and the average was 17 mm. Hg.

Patient 1 (Table I) had right-heart catheterization two months after pericardectomy. He improved clinically over a period of 12 months, but catheterization was not repeated until 62 months later. Although the pressure values in the right side of the heart remained elevated, they were lower than at the time of the first measurement. There was no difference between the right-atrial mean and the pulmonary-arterial diastolic pressures in either instance. The pulmonary-arterial wedge pressure, which approximates the left-atrial pressure,[16] was equal to the right-atrial mean pressure. In Figs. 1 and 2, the pressure tracings are shown for each catheterization. The early diastolic dip and high diastolic plateau are present in the right ventricular tracing in each.

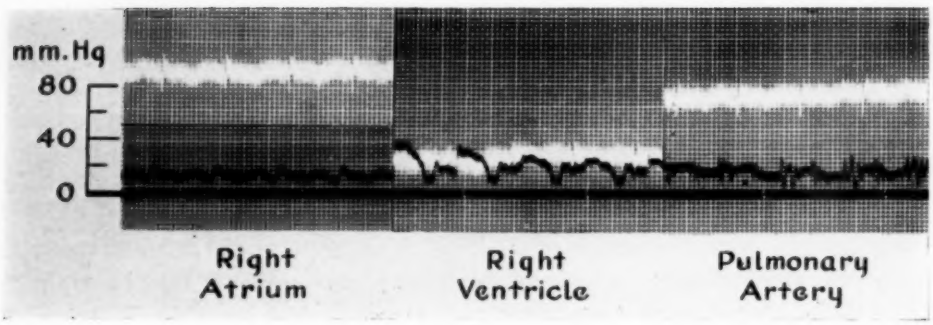


Fig. 1.—The pressure tracing of patient 1, Table I, two months after surgery.

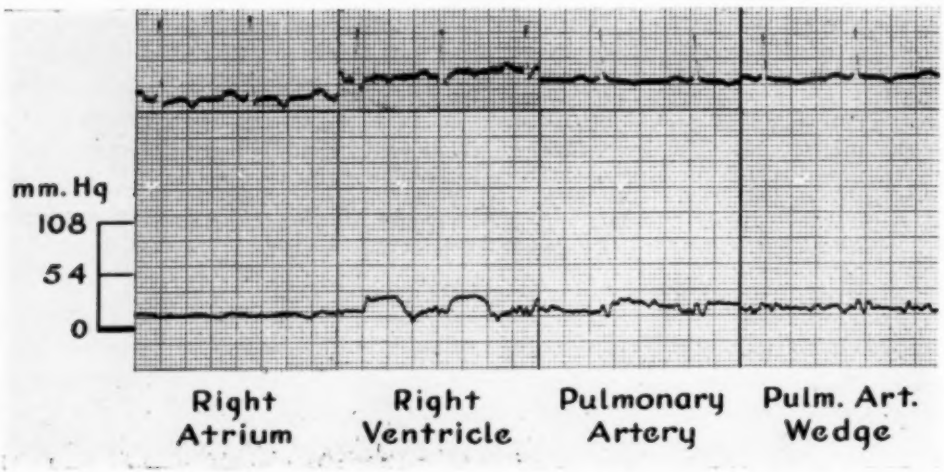


Fig. 2.—The pressure tracing of patient 1, Table I, 62 months after surgery.

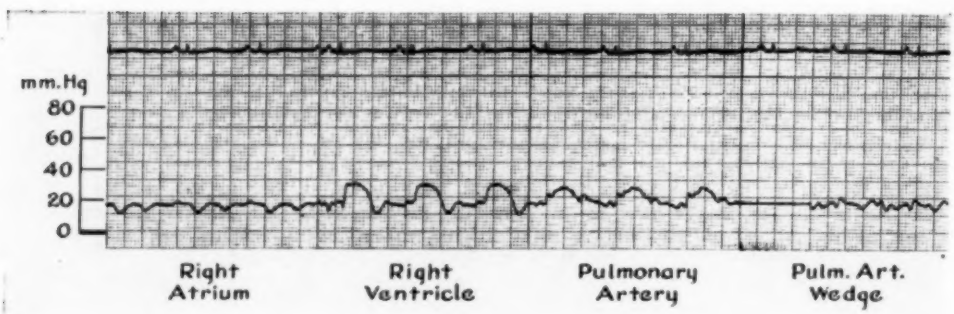


Fig. 3.—The pressure tracing of patient 8, Table I, before surgery.

Figs. 3 and 4 are the pressure tracings of Patients 8 and 9 (Table I) who had small hearts with no calcification of the pericardium but other classical signs of constrictive pericarditis. Both patients had thick, chronically inflamed pericardia at surgery.

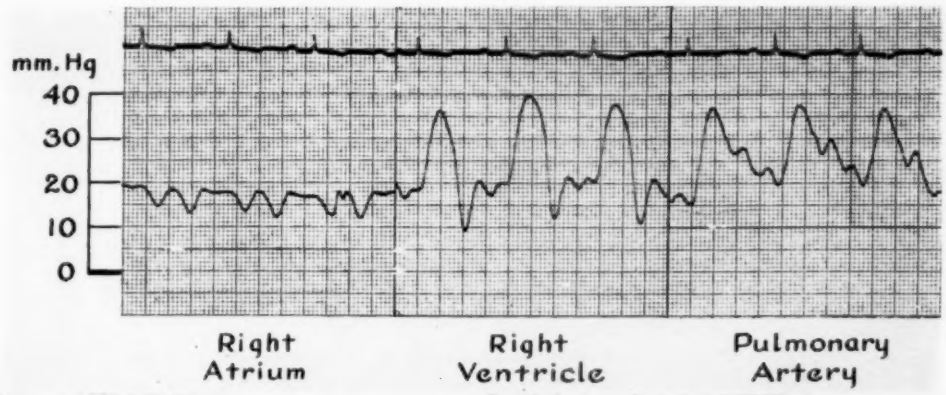


Fig. 4.—The pressure tracing from patient 9, Table I, showing a marked variation in the pulmonary arterial pressure with respiration.

The pulmonary arterial wedge pressure in Fig. 5, Patient 3 (Table I), was elevated to the same level as the right-atrial mean pressure and increased significantly with respiration due to accompanying pulmonary disease. This tracing demonstrates again the marked decrease in the difference between the

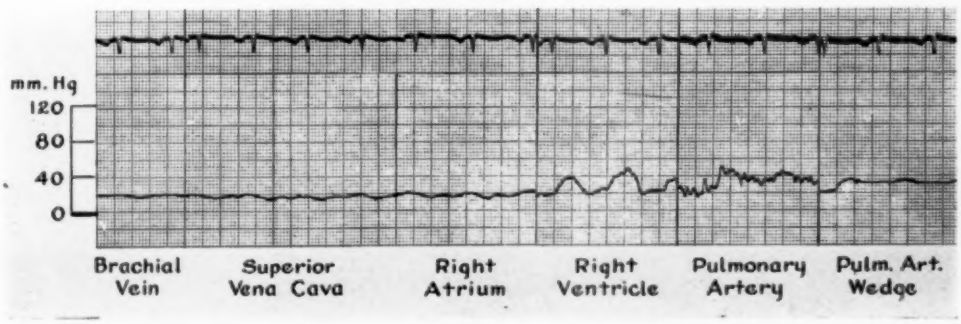


Fig. 5.—The pressure tracing of patient 3, Table I.

right-atrial mean and pulmonary-arterial diastolic pressures in constrictive pericarditis. At the time of thoracotomy, just before pericardectomy, a needle attached to a pressure-recording system was inserted into the left atrium and ventricle. The pressure tracings obtained are shown in Fig. 6. The diastolic dip was absent. The left-atrial mean pressure was 20 mm. Hg, and the left-ventricular diastolic pressure 20 mm. Hg.

Patient 13 (Table I) had acute pericardial effusion with tamponade. The pressures were measured in the superior vena cava, right atrium, right ventricle,

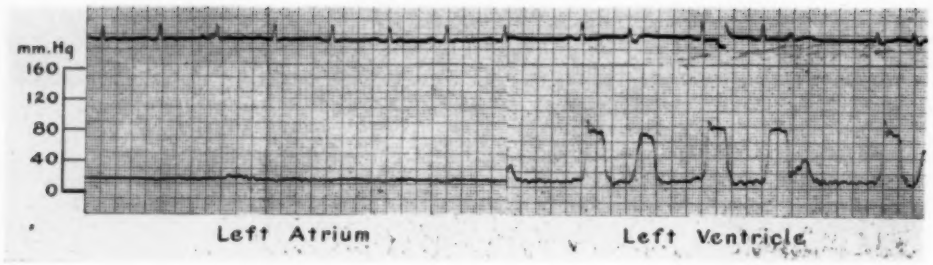


Fig. 6.—The pressure tracing taken from the left atrium and left ventricle in patient 3, Table I, during thoracotomy, before pericardectomy.

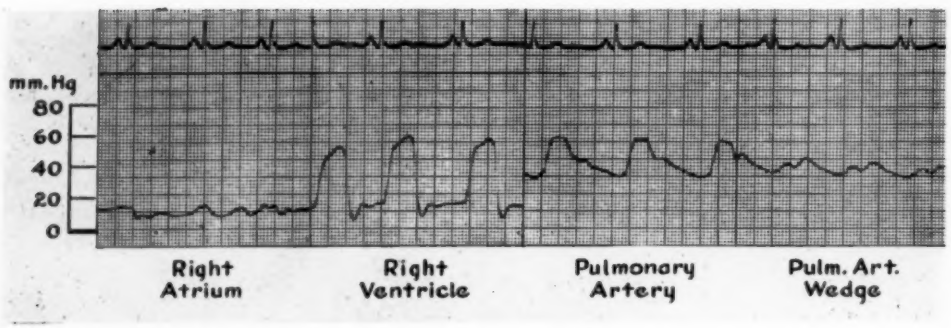


Fig. 7.—The pressure tracing from a patient with severe mitral stenosis showing an early diastolic dip and elevated right-atrial and ventricular diastolic pressures with right-heart failure.

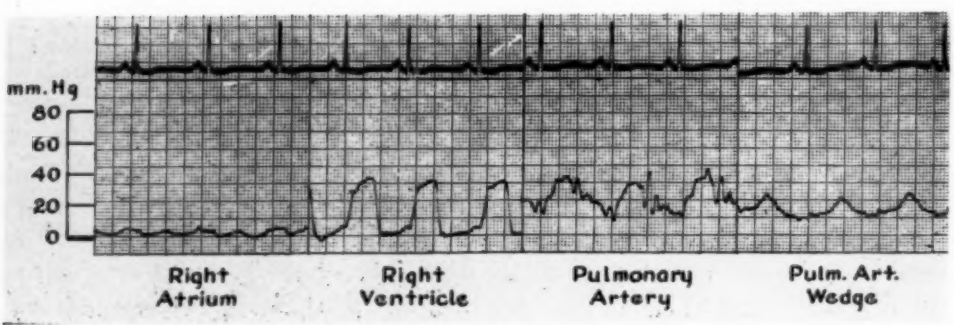


Fig. 8.—The pressure tracing from the same patient as that in Fig. 7 after mitral valvotomy. Note the absence of the dip and diastolic plateau with return of the atrial and ventricular diastolic pressures to the normal level.

and the pulmonary artery. The catheter was inserted into a small pulmonary artery to obtain the wedge pressure. Following removal of the pericardial fluid, pressures were again measured. The diastolic pressures in the various chambers of the right side of the heart fell to within 3 mm. Hg of the normal range. The wedge pressure fell to the level of the right-atrial pressure.

The ratio of the right-ventricular end-diastolic to systolic pressure was greater than 40 per cent in all patients with constrictive pericarditis and pericardial effusion. The range of the ratios was 40 to 61 per cent. In the group of patients with pericardial disease the difference between the right-atrial mean and pulmonary-arterial diastolic pressures was reduced to a range of 0 to 5 mm. Hg with an average difference of 1.0 mm. Hg. The patients with pericardial disease all had peripheral signs similar to right-heart failure, and 92.3 per cent had a diastolic dip (12 of 13 patients). One patient with pericardial effusion did not have a dip.

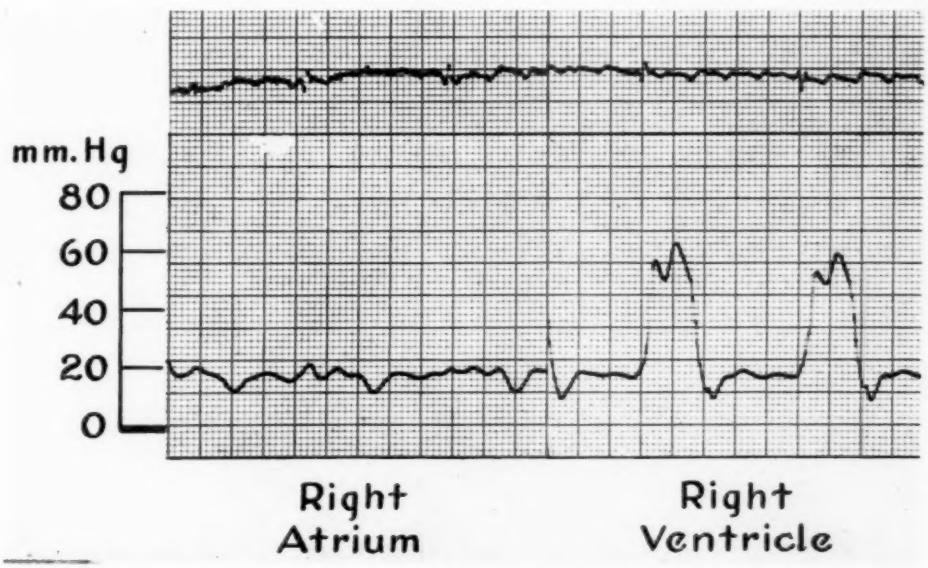


Fig. 9.—The pressure tracing from a patient with idiopathic myocarditis and right-heart failure.

A diastolic dip and high-diastolic pressure plateau were found in a small number of the patients with cardiac disease other than pericarditis.

Fig. 7 is the pressure tracing of a patient with severe rheumatic mitral stenosis and right-heart failure. The difference between the pulmary-arterial diastolic and right-atrial mean pressures was 10 mm. Hg. The ratio of the right-ventricular end-diastolic pressure to systolic pressure was 20 per cent. In Fig. 8 is shown the tracing following mitral valvotomy. The diastolic pressures in the right atrium and ventricle fell to a normal level, and the diastolic dip was not present.

A patient with idiopathic myocarditis and severe cardiac failure, Fig. 9, was found to have a diastolic dip and a high diastolic plateau. The ratio was 30 per cent.

Fig. 10 is the pressure tracing of a patient with an interatrial septal defect and severe right-heart failure. An early right-ventricular diastolic dip and high-diastolic pressure plateau were present. The ratio was 25 per cent. The difference between the right-atrial mean and pulmonary-arterial diastolic pressures was 10 mm. Hg.

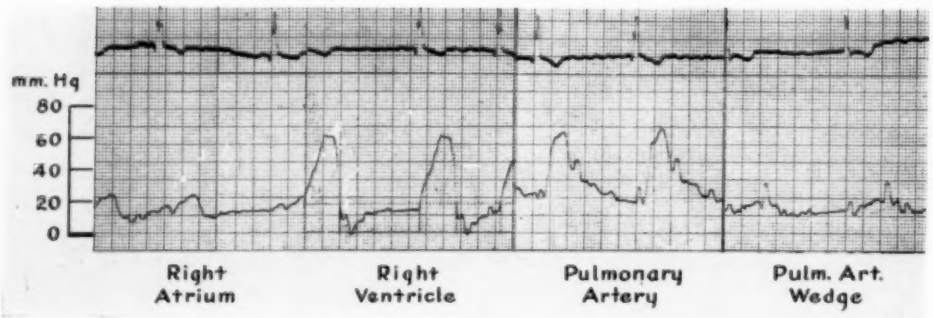


Fig. 10.—The pressure tracing from a patient with an interatrial septal defect and right-heart failure.

The right-ventricular diastolic dip and high-diastolic pressure plateau are shown in the pressure tracing of a patient with primary pulmonary arteriolosclerosis (Fig. 11). The ratio was 15 per cent. The difference between the right-atrial mean and pulmonary-arterial diastolic pressures was 25 mm. Hg.

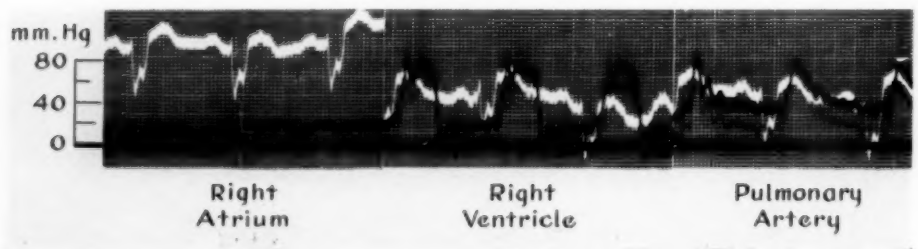


Fig. 11.—The pressure tracing from a patient with primary pulmonary arteriolosclerosis and right-heart failure.

In Table II are recorded the cardiac-catheterization data from 453 patients with cardiac disease of nonpericardial origin. Of this group, 286 patients had congenital cardiac disease and sixty-two (22 per cent) had had right-heart failure. Seven of the sixty-two patients (11 per cent) had right-ventricular end-diastolic to systolic pressure ratios of more than 40 per cent. The four patients who had a significant diastolic dip all had right-heart failure. The range of diastolic-to-systolic pressure ratios is shown.

TABLE II. RIGHT HEART CATHETERIZATION DATA FROM PATIENTS WITH CARDIAC DISEASE OTHER THAN PERICARDIAL DISEASE

DIAGNOSIS	NO. OF PATIENTS	NO. WITH RIGHT-HEART FAILURE	RANGE OF RATIO %	NO. WITH RATIO OF 40% OR OVER	NO. WITH A DIASTOLIC DIP	NO. WITH DIASTOLIC DIP AND RIGHT-HEART FAILURE	NO. WITH DIASTOLIC DIP AND RATIO OF 40% OR OVER
Congenital heart disease							
Pulmonary stenosis	42	11	2–80	3	2	2	1
Interventricular septal defect	37	5	1–31	0	0	0	0
Tetralogy of Fallot	37	10	1–50	1	0	0	0
Patent ductus arteriosus	36	6	3–38	0	0	0	0
Pulmonary stenosis with interatrial septal defect	31	9	1–60	1	1	1	0
Interatrial septal defect	27	4	5–29	0	1	1	0
Eisenmenger complex	19	4	2–18	0	0	0	0
Miscellaneous	57	13	2–80	2	0	0	0
Mitral stenosis	113	61	1–60	2	8	8	1
Pulmonary emphysema	27	13	2–24	0	0	0	0
Miscellaneous adult cardiac disease	15	9	2–80	2	4	4	0
Pericardial disease	13	13	40–61	13	12	12	12
Normal persons	14	0	5–18	0	0	0	0

TABLE III. A COMPARISON OF THE RIGHT HEART CATHETERIZATION DATA IN 14 NORMAL PERSONS, 13 PATIENTS WITH PERICARDIAL DISEASE, AND 37 PATIENTS WITH RIGHT HEART FAILURE BECAUSE OF OTHER FORMS OF CARDIAC DISEASE

TYPE OF PERSON	NO. OF PATIENTS	CARDIAC INDEX (L./SQ.M.)	MEAN RIGHT-ATRIAL PRESSURE (MM. HG)	END RIGHT VENTRICULAR DIASTOLIC PRESSURE (MM. HG)	PULMONARY ARTERY DIASTOLIC PRESSURE (MM. HG)	DIFFERENCE BETWEEN RIGHT ATRIAL MEAN AND PULMONARY ARTERIAL DIASTOLIC PRESSURES (MM. HG)	RANGE OF DIFFERENCE
Normal	14	4.1	3	3	9	6	4–8
Constrictive pericarditis (3 with acute effusion)	13	2.28	18	17	19	1	0–5
Right-heart failure	37	—	9	8	32	23	0–49

In the group of 113 patients with mitral stenosis, sixty-one (53 per cent) had right-heart failure. Two of the sixty-one had a ratio of more than 40 per cent, and eight had a significant diastolic dip. All of these patients had right-heart failure.

Thirteen of twenty-seven patients with pulmonary emphysema had right-heart failure. None of this group of patients had an elevated ratio or a diastolic dip.

Nine of fifteen patients with miscellaneous forms of cardiac disease had right-heart failure. Four of those with right-heart failure had a diastolic dip.

In the total group of patients with cardiac lesions other than pericardial disease, there were 145 patients (32 per cent) with right-heart failure at the time of cardiac catheterization. The diastolic dip was present in sixteen (3.5 per cent) of this group. It was not present in those without right-heart failure. The dip was present in only two patients having a right-ventricular diastolic-to-systolic pressure ratio of over 40 per cent.

In Table III are listed the pressured differences between the pulmonary-arterial diastolic and mean right-atrial pressures in the group of patients with pericardial disease and other forms of cardiac lesions. The range of this pressure difference separated the groups in most instances. Only one of the normal group and two of the group with right-heart failure had a pressure difference which fell within the range of those with pericardial disease. The data for normal persons are also listed.

DISCUSSION

The basic lesion causing the pathologic physiology of constrictive pericarditis and pericardial effusion is constriction of the ventricles.[14,15]

The absence of a significant pressure difference between the right-atrium and peripheral venous channels in all cases precludes the theory of inflow stasis because of constriction about the base of the large veins emptying into the right atrium. In the one patient in which the pressure in the left atrium was measured, the wedge pressures and the pressure of the blood in the right atrium were in the same order of magnitude. These observations would indicate that no physiologic constriction of the pulmonary veins occurred in the patients with constrictive pericarditis or pleural effusions. There was no demonstrable anatomic constriction of the pulmonary veins or venae cavae found at surgery. Systolic ejection is impaired and the stroke volume decreased[16] because of an adherent pericardium and atrophic myocardium. Maximal filling of the ventricle occurs in the first one-third of diastole. There is little or no increase in the quantity of blood in the right ventricle during the latter two-thirds of the diastolic-filling period. The cardiac output is increased by an increase in the cardiac rate per minute. The impaired diastolic filling of the ventricles and the diminished cardiac output are responsible for all of the abnormal physiologic changes observed in constrictive pericarditis and pericardial effusion. The decreased cardiac output and increased elastic resistance to ventricular diastolic filling leads to an elevation of the intracardiac and peripheral venous pressures.

As the severity of the constrictive lesion increases, the cardiac output progressively decreases, the intracardiac and peripheral venous pressure increases and the difference in pressure normally observed in the various cardiac and vascular chambers tends to disappear. It is now well established that these hemodynamic changes are the same in the right side and left side of the heart in pericardial disease.[14,15]

In the presence of a limited ventricular-filling capacity, increased resistance to filling by the highly elastic pericardium, and increased filling pressure, the ventricle is filled maximally early in diastole. These factors cause the apparent dip and the high end-diastolic plateau in the right-ventricular pressure tracing. Removal of pericardial fluid alters the effects of tamponade as shown in Table I, Patient 13. The diastolic pressures in the right atrium and ventricle fell to almost normal levels. The wedge pressure fell to a point within the normal range. These data indicate that constriction of the heart causes an elevation of pressure in all cardiac chambers and in the pulmonary vascular bed.

The right-ventricular systolic pressure is normal or slightly elevated in pericardial disease. The right-ventricular diastolic pressure is elevated to a relatively greater degree, therefore the ratio of the diastolic to systolic pressure is high.

The M or W configuration in the right atrial pressure tracing is caused by two sudden falls in pressure. The first is the result of rapid atrial emptying, and the second is due to right-ventricular contraction.

The characteristic features of the pressure-tracing curves seen in pericardial disease occur far less frequently in other forms of cardiac disease with right-heart failure. In these patients, in contrast to those with constrictive pericarditis, the right ventricle is dilated, the cardiac output diminished, and the residual right-ventricular blood volume is increased. The defect in this situation has to do solely with diminution in output and not, as in constrictive pericarditis, with decreased ventricular filling along with decreased output.

SUMMARY

The pressure tracings obtained by right-heart catheterization are described in ten patients with constrictive pericarditis and three patients with acute pericardial effusion. The left-atrial and ventricular-pressure tracing of one of these is shown. The cardiac catheterization data of 453 patients with other forms of cardiac disease were reviewed.

CONCLUSIONS

The cardiac index was reduced in all patients with constrictive pericarditis.

The right-ventricular diastolic-to-systolic pressure ratio was greater than 40 per cent in all patients with constrictive pericarditis. This was true in only 2.4 per cent of 453 patients with cardiac disease other than constrictive pericarditis. In the latter group only 0.7 per cent had the combination of the dip and high ratio, whereas this occurred in 92 per cent of the patients with pericardial disease.

The difference between the pulmonary-arterial diastolic and right-atrial mean pressures was consistently diminished in patients with pericardial disease, but this was observed less frequently in those with other forms of cardiac disease with right-heart failure.

The early rapid rise in the diastolic-filling pressure to form a plateau in the right-ventricular pressure tracing is characteristic but not specific for constrictive pericarditis.

REFERENCES

1. Bloomfield, R. A., Lauson, H. D., Cournand, A., Breed, E. S., and Richards, D. W., Jr.: Recording of Right Heart Pressure in Normal Subjects and in Patients With Chronic Pulmonary Disease and Various Types of Cardio-Respiratory Disease, J. Clin. Investigation **25**:639, 1946.
2. Hansen, A. T., Eskildsen, P., and Gøtzsche, H.: Pressure Curves From the Right Auricle and the Right Ventricle in Chronic Constrictive Pericarditis, Circulation **3**:881, 1951.
3. Wood, E. H., Geraci, J. E., Pollack, A. A., Groom, D., Taylor, B. E., Pender, J. W., and Pugh, D. G.: General and Special Technics in Cardiac Catheterization, Proc. Staff Meet., Mayo Clin. **23**:494, 1948.
4. Hetzel, P. S., Wood, E. H., and Burchell, H. B.: Pressure Pulses in the Right Side of the Heart in a Case of Amyloid Disease and in a Case of Idiopathic Heart Failure Simulating Constrictive Pericarditis, Proc. Staff Meet., Mayo Clin. **28**:89, 1953.
5. McKusick, V. A.: Chronic Constrictive Pericarditis. I. Some Clinical and Laboratory Observations, Bull. Johns Hopkins Hosp. **90**:3, 1952.
6. Yu, P. N. G., Lovejoy, F. W., Joos, H. A., Nye, R. E., and Mahoney, E. B.: Right Auricular and Ventricular Pressure Patterns in Constrictive Pericarditis, Circulation **7**:102, 1953.
7. Cournand, A., Riley, R. L., Breed, E. S., Baldwin, E. De F., and Richards, D. W., Jr.: Measurement of Cardiac Output in Man Using the Technique of Catheterization of the Right Auricle or Ventricle, J. Clin. Invest. **24**:106, 1945.
8. Wilson, R. H., McKenna, W. T., Jensen, N. K., Johnson, F., and Dempsey, M. E.: The Significance of the Pulmonary Arterial Wedge Pressure, J. Lab. & Clin. Med. **42**:408, 1953.
9. Lyons, R. H., Kennedy, T. A., and Burwell, C. S.: Measurement of Venous Pressure by the Direct Method, Am. Heart J. **16**:675, 1938.
10. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and by Manometric Measurement, J. Biol. Chem. **61**:523, 1924.
11. Fick, A.: Ueber die Messung des Blutquantums in den Herzventrikein, Verhandl. d. Phys. Med. Gesellsch. Z. Wurzburg **2**:16, 1870.
12. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Vol. 2, Methods, Baltimore, 1943, Williams & Wilkins Company.
13. Wilson, R. H.: pH of Whole Arterial Blood, J. Lab. & Clin. Med. **37**:129, 1951.
14. Isaacs, J. P., Carter, N. B., II, and Haller, J. A., Jr.: Experimental Pericarditis: The Pathologic Physiology of Constrictive Pericarditis, Bull. Johns Hopkins Hosp. **90**:259, 1952.
15. Metcalfe, S. M., Woodbury, T. W., Richards, V., and Burwell, C. S.: Studies in Experimental Tamponade: Effects on Intravascular Pressure and Cardiac Output, Circulation **5**:518, 1952.
16. Harvey, R. M., Ferrer, M. I., Cathcart, R. T., Richards, D. W., Jr., and Cournand, A.: Mechanics and Myocardial Factors in Chronic Constrictive Pericarditis, Circulation **8**:695, 1953.

THE CLINICAL FEATURES OF AORTIC STENOSIS

AVARD M. MITCHELL, M.D.,* CHARLES H. SACKETT, M.D.,**
WARREN J. HUNZICKER, M.D., *** AND
SAMUEL A. LEVINE, M.D.

BOSTON, MASS.

CRITERIA for the diagnosis of aortic stenosis in the past have varied greatly. At one time, a systolic murmur at the base of the heart alone was required, but it was soon recognized that many cases with this auscultatory finding had no organic lesion of the aortic valve. At another stage of cardiologic knowledge it was the custom to make the diagnosis only when a basal systolic thrill was present, but valvular calcification by x-ray and stenosis at post-mortem examination have been shown to exist without a systolic thrill and even in the presence of only a slight murmur or none at all. In a sense, the diagnosis was of less practical importance in the past than it is now, since no treatment was available to alter the obstructing lesion. This is no longer true. Great strides in cardiac surgery are being made, and it is possible that the repair and relief of a stenosis of the aortic valve may be accomplished with reasonable safety in the near future. Thus the internist is confronted with a new challenge, for he must learn how to evaluate more precisely the degree and physiologic significance of an obstructing lesion in that area in order to judge whether indications for surgery exist. It is, therefore, important to know in more accurate detail the exact clinical course of the disease. At what stage and on what evidence can the diagnosis of aortic stenosis be made? How frequently and how early in the course of the disease does calcification become evident by fluoroscopic examination? Is the presence or absence of an aortic second sound helpful in estimating the degree of stenosis of the aortic valve? What influence has the blood pressure on the course of the disease? Are other valvular lesions or coronary artery disease present in addition, and how do they affect the prognosis? How long may patients with aortic stenosis be expected to live after the onset of angina, syncope, or congestive heart failure? Such questions are no longer academic, but need to be answered so that the clinician may profit fully from the recent rapid advances in surgery of the heart. Therefore, it is our purpose to review and delineate as clearly as possible the clinical features of aortic stenosis with these objectives in mind.

From the Medical Clinic of Peter Bent Brigham Hospital and the Department of Medicine, Harvard Medical School, Boston, Mass.

This study was aided in part by the Charles E. Merrill Cardiac Research Fund.

Received for publication May 21, 1954.

*Research Fellow in Medicine of the American College of Physicians, 1952-53.

**Heart Trainee of the National Heart Institute, U. S. Public Health Service, 1953-54.

***Heart Trainee of the National Heart Institute, U. S. Public Health Service, 1952-53.

It is not the purpose of this investigation to review the extensive literature pertaining to the problems of aortic stenosis. There have been various contributions in the past decades that have added considerably to our knowledge.[1-16] They have called our attention to certain peculiarities of the problem such as the occurrence of syncope, the frequency with which calcification of the valve can be seen fluoroscopically, the type and transmission of the systolic murmur, the occurrence of angina and sudden death, and other aspects of the clinical course of the disease. What is needed at the present is a detailed review of many of these various features, with consideration given to the possible selection of cases for valvular surgery.

SCOPE OF THE STUDY

All Peter Bent Brigham Hospital records from 1913 to 1952 were reviewed. It was our objective to include only cases of indubitable aortic stenosis occurring alone or in combination with other cardiac lesions, valvular or otherwise. Three types of cases were included. The first category was that of aortic stenosis proved at autopsy and therefore involves no error whatever. Calcification was present in many but not all of these valves. The second group was composed of patients in whom the diagnosis of aortic stenosis was made clinically and verified by the demonstration of calcium in the region of the aortic valve by x-ray and fluoroscopic study. In this hospital the possible error in diagnosing aortic stenosis under these circumstances is very small. It is clear that calcification takes many years to develop, and therefore valvular narrowing exists for a long period of time before calcium is present or visible. This is borne out at post mortem by the finding of stenosed but uncalcified valves; also, many hospital cases with the classical clinical findings were excluded because they were not corroborated by autopsy or by x-ray demonstration of calcification. However, in order to have a broader spectrum of this condition and to embrace those cases that were ambulatory, patients seen by one of us (S.A.L.) in his private practice and considered to have unquestionable aortic stenosis on the bases of clinical appraisal were included as a third category. Criteria here included a history of rheumatic fever, an enlarged left ventricle, a basal systolic murmur, basal thrill, diminished aortic second sound, normal sinus rhythm with cardiac symptoms, and so forth. Not all the above findings were present, but the total survey led to the clinical diagnosis. It must be admitted that there is a diagnostic error in this group, but we do not believe it is very great.

Though post-mortem data are extremely reliable in the determination of valvular stenosis, the estimation of insufficiency by this examination is much less certain. It is our feeling that the clinical diagnosis of valvular insufficiency as evidenced by an aortic diastolic (aortic valve) or a loud apical systolic murmur (mitral valve) is somewhat more reliable. Clinical data and autopsy findings were appraised and a final diagnosis assigned to each case on the basis of all the information available.

A total of 533 cases of aortic stenosis were included in this study, made up of 214 confirmed at autopsy, 158 in which the clinical diagnosis was substantiated by demonstration of calcification of the aortic valve by x-ray, and 161 in whom the diagnosis rested on the strongly convincing clinical findings mentioned here.

CLASSIFICATION OF LESIONS

Definite criteria were used for diagnostic classification of the 533 cases in the study. Cases were labeled pure aortic stenosis and will be referred to as such throughout this paper, if there was no diastolic murmur present, and/or on post-mortem, x-ray, or clinical examination no evidence of any other valvular disease was found. The diagnosis of aortic stenosis and insufficiency depended on the presence of a definite decrescendo murmur in diastole at the aortic area or along the upper left sternal border, along with the criteria for aortic stenosis previously described. Similarly, accompanying lesions of the mitral and tricuspid valves were also diagnosed in the presence of appropriate post-mortem, x-ray, or clinical findings.

TABLE I. CLASSIFICATION OF LESIONS

	AUTOPSY		X-RAY		CLINICAL		TOTAL
	WITHOUT SBE	WITH SBE	WITHOUT SBE	WITH SBE	WITHOUT SBE	WITH SBE	
AS	29		46		54	2	131
ASAI	30	18	60	1	34	1	144
ASMI	3		4		14		21
ASAIMI	8	5	13	1	31	1	59
Total ASAI	41	23	77	2	79	2	224
ASMS	7	3	1				11
ASAIMS	9		5		4		18
ASMSMI	4	1	3		4		12
ASAIMSMI	47	12	24		15	1	99
ASAIMSMITI	8	1					9
Total ASMS	75	17	33		23	1	149
ASAIMSMITS	17	3					20
ASAIMSMITSTI	5						5
ASMSMITS	1						1
ASAIMIMSTSPS	2						2
ASAIMITS	1						1
Total ASMSTS	26	3					29
Grand Total	171	43	156	2	156	5	533

AS = aortic stenosis; AI = aortic insufficiency; MS = mitral stenosis; MI = mitral insufficiency; TS = tricuspid stenosis; TI = tricuspid insufficiency; PS = pulmonic stenosis; SBE = subacute bacterial endocarditis.

Table I lists the various diagnostic categories. Throughout the subsequent discussion, the numerous subheadings will be referred to in four main subgroups, as shown in Table I. These are aortic stenosis (pure, AS), aortic stenosis and insufficiency without mitral stenosis (ASAI), aortic and mitral stenosis with or without insufficiency of these valves (ASMS), aortic, mitral and tricuspid stenosis with or without other lesions (ASMSTS). Of the total 533 cases in this study, 275 (52 per cent) had lesions of the aortic valve alone. There were 131 cases of

pure aortic stenosis (25 per cent) and 144 of aortic stenosis and insufficiency (27 per cent). Thus about one-half of those with aortic stenosis without mitral stenosis had an accompanying diastolic murmur. Some of the cases with the diagnosis of aortic stenosis, aortic and mitral insufficiency may well have been just aortic stenosis and insufficiency. One is inclined to doubt that the combined lesion of aortic stenosis, aortic and mitral insufficiency occurs as frequently as the figures would indicate, since it is often difficult to decide whether the apical systolic murmur is merely transmitted from the aortic area when the murmur of aortic stenosis is loud. By using these additional cases, there were 355 cases of aortic stenosis without mitral stenosis or 67 per cent of the series. An additional mitral stenosis was present in 178 cases with or without mitral insufficiency (33.2 per cent) and of these, twenty-nine also had tricuspid stenosis. This latter group made up only 5 per cent of the total. It is of further interest that the diagnosis of aortic insufficiency was made in 357 cases or 67 per cent. Inasmuch as aortic insufficiency was diagnosed by the presence of a diastolic murmur at the left sternal border, some of these cases may have been instances of a Graham-Steele murmur rather than actual aortic incompetence.

ETIOLOGY

There is still some confusion as to the cause and pathologic development of stenosis and calcification of the aortic valve. The opinion of pathologists regarding this process has varied widely from time to time, and not very long ago they regarded most of the cases as arteriosclerotic in origin. Clinicians were early aware of the error of this view and have held to the opinion that a previous rheumatic infection was responsible for the development in later years of constriction of the aortic valves in many instances. They have been puzzled that calcification of the mitral valve was readily acknowledged as a sequel of rheumatic fever while calcium in the aortic valve was often said to be arteriosclerotic in origin. It has long been known that calcification often follows infection or trauma of various parts of the body, whether as a gumma, tubercle, ecchinococcus cyst, glioma, hemorrhage, etc., as well as a rheumatic infection of a valve.

Most pathologists now feel that a distinction can be made between arteriosclerotic and rheumatic valvular lesions by the nature of the findings at autopsy. Extensive calcium deposition may occasionally occur in the valvular area in the absence of any stenosis. However, if rheumatic fever is responsible, calcification of the ring extends to the free margin of the valve cusps, while arteriosclerotic calcification does not go as far into the valvular area. Furthermore, actual fusion of contiguous cusps is much more likely to indicate a rheumatic rather than arteriosclerotic etiology. Today 90 to 95 per cent of the stenotic lesions of the aortic valve in this geographic area are thought to be rheumatic or infectious in origin.[17]

It is interesting to speculate concerning some of the cases of aortic stenosis in which there is no definite past history of rheumatic fever. A rare case may have been born with it and really have congenital aortic stenosis. In others, there are enough subsidiary stigmata of rheumatic infection such as early growing pains, epistaxis, family history of rheumatic fever or rheumatic heart disease to

make one strongly suspect that that individual is rheumatic. It is well known that individuals may have a simple sore throat without any joint manifestations and yet develop some rheumatic valvular disease directly after the initial infection. In many instances when no history of rheumatic fever could be obtained, it was learned that no murmur was ever audible during infancy and early childhood and that at the age of fifteen or more, a systolic murmur was first detected. When such a patient is seen at the age of 50 or 60 with classical calcific aortic stenosis, it is difficult to imagine that the arteriosclerotic process began at the age of twenty despite the fact that pathologists formerly called the condition Mönckeberg's sclerosis of the aortic valve. The situation need not be any different if the murmur first appeared at the age of 40 or so. There is reason to strongly suspect that apparently minor infections, probably streptococcal in nature, without any joint manifestations, but occurring even in middle age or later may initiate a reaction in the aortic valve that leads to aortic stenosis just as it does in childhood when obvious rheumatism is more often present. One may look upon such individuals as having had a rheumatic response in the heart to an infection that otherwise would be quite benign. The eventual calcification can be regarded as a secondary change, the result of the chronic inflammation and trauma as in other pathologic conditions.

The diagnosis of syphilis was made in twenty of the 533 patients in the series, either on the basis of a positive serologic test or of pathologic evidence of syphilitic aortitis. It does not follow that a positive blood test means that the heart disease found was syphilitic in origin. In fact, of the ten cases that were examined post mortem, only four showed signs of syphilitic aortitis. Three of these four had a past history of rheumatic fever. If cases are eliminated who had a rheumatic history or who showed mitral stenosis at autopsy, then there was only one definite and two other possible instances of aortic stenosis that also showed syphilitic aortitis. It is difficult to decide from a pathologic point of view whether or not the stenosis of the aortic valve was originally syphilitic (with subsequent calcification) in those cases who had a rheumatic history or showed mitral stenosis, even if classical syphilitic aortitis was present. It is possible that in those doubtful cases, the stenosis of the aortic valve was still due to a nonsyphilitic or rheumatic infection even when there were other stigmata of syphilis. It can be safely stated that if syphilis causes aortic stenosis, it is a very rare clinical event.

PAST HISTORY OF RHEUMATIC FEVER

Of the entire 533 cases, there was a definite history of rheumatic fever in 37 per cent, and a suggestive history of growing pains, rheumatism, or frequent epistaxis in an additional 11 per cent (Table II). Less than 2 per cent had had chorea, and 3 per cent gave a history of scarlet fever. It is of interest that the 131 cases of pure aortic stenosis had a much lower incidence of known attacks of rheumatic fever than any of the other categories. The figures for the four main groups were pure aortic stenosis 15 per cent, aortic stenosis and insufficiency 34 per cent, aortic and mitral stenosis 54 per cent, and trivalvular stenosis 59 per cent. If the cases of pure aortic stenosis are excluded, the contrast is more striking, for 44 per cent of the remaining 402 cases had a definite history of

rheumatic fever and another 13 per cent had a suggestive history. This lower incidence of a rheumatic history lends support to the possibility that some cases of pure aortic stenosis may be of an arteriosclerotic origin.

SEX DISTRIBUTION

Of the 533 cases 318 were males (60 per cent). When the aortic valve alone was involved, two-thirds of the cases were males. Among those examined post mortem, this figure was 81 per cent. In the group diagnosed by x-ray the figure was 71 per cent and dropped to 53 per cent in the clinical group. In the 149 cases with bivalvular stenosis involving both the aortic and mitral valves with or without valvular insufficiency, there were seventy-five males (50 per cent). Males, however, made up only 24 per cent of the twenty-nine cases in which there was stenosis of all three valves (aortic, mitral, and tricuspid). Thus males predominated among the cases of stenosis of the aortic valve alone. If aortic and mitral stenosis were concomitantly present, males and females were equally affected. In trivalvular lesions, however, there were about three female patients for every male.

LIFE EXPECTANCY

A great increase in the life expectancy of the general population has occurred during the 40-year interval from 1913 to 1953 in which the 533 patients of this study were seen. The patient with heart disease also has a longer life span now than in 1913. He may survive noncardiac ailments that formerly would have proved fatal, to succumb later to his cardiac lesion. Some of the earlier cases of aortic stenosis in this series would undoubtedly have had a better clinical course as a result of present-day therapeutic agents and medical knowledge. However, all but 10 per cent of the 533 were seen later than 1930, so that the great majority of patients lived during the time when mercurial diuretics were employed in treatment. Furthermore, a good number were observed after 1945 when penicillin and other antibiotics became available.

The age at death is known for 326 of the 533 patients (61 per cent), the average age being 52.2 years. The average was greatest for pure aortic stenosis at 65.3 years (63 cases). With aortic stenosis and insufficiency but without mitral stenosis the average age at death was 52.5 years (123 patients), for stenosis of both the aortic and mitral valves this average was 48.4 years (111 patients) and for stenosis of the aortic, mitral, and tricuspid valves the average was 36.5 years (29 patients).

Males made up 191 or 57.5 per cent of the 326 patients for which the age at death was known, and the average age at death of males was 53.1 years and of females 51.0 years. The total general average is lower for females because they predominated so heavily (22 to 7) in the group of trivalvular lesions in which death occurred at such an early age. There was only a slight difference of a year or so between the age at death of each sex in the individual subgroups. Whenever the age at death of a patient was not known, the age at the time last seen was recorded. The average for 126 males was 51.8 years, and for eighty-one females was 55.0 years. The ages when last seen for the various groups was found to be slightly lower than the corresponding age at death (Table II).

TABLE II. SUMMARY OF DATA

			AS	ASAI	ASMS	ASMSTS	TOTAL
PAST HISTORY OF RHEUMATIC FEVER		No.	20	76	79	20	195
		%*	15.3	33.8	53.6	58.6	36.9
SEX	MALES	No.	79	157	75	7	318
		%*	60.3	70.1	50.1	24.1	59.7
	FEMALES	No.	52	67	74	22	215
		%*	39.7	29.9	49.9	75.9	40.3
AGE AT DEATH	TOTAL SERIES	No.	63	123	111	29	326
		Av. age	65.3	52.5	48.4	36.5	52.2
	WITH RHEUMATIC FEVER	No.	5	27	—	—	—
		Av. age	63.2	52.9	—	—	—
	WITHOUT RHEUMATIC FEVER	No.	58	57	—	—	—
		Av. age	65.8	52.6	—	—	—
AGE LAST SEEN		No.	68	101	38	0	207
		Av. age	60.8	50.7	44.9	0	52.9
DURATION OF CONGESTIVE FAILURE		No.	37	71	73	18	199
		Av. mos.	22	28.9	56.4	80.0	42.5
		Range	1 wk.-10 yr.	1 mo.-17 yr.	1 mo.-17 yr.	1 mo.-18 yr.	1 wk.-18 yr.
INTERVAL BETWEEN R.F. AND CONG. FAILURE		No.	17	64	71	21	173
		Yr.	47.6	34.2	28.2	14.6	31.0
ANGINA PECTORIS	INCIDENCE	No.	48	78	30	3	159
		%*	36.7	34.8	20.8	10.4	29.8
	AGE AT ONSET	Yr.	61	49.5	49.3	32	53
	DURATION	Yr.	4.0	4.1	4.2	3.3	4.1
	DEGREE OF STENOSIS	No.	6	21	19	3	49
		Av.	2.6	3.2	3.1	3.0	3.0
SYNCOPE	INCIDENCE	No.	27	24	15	1	67
		%*	20.6	10.7	10.0	3.5	12.6
	DURATION	No.	27	19	12	1	59
		Yr.	3.0	3.7	3.1	5.0	3.3
	DEGREE OF STENOSIS	No.	3	3	10	0	16
		Av.	3.0	3.3	3.1	0	3.1

TABLE II. SUMMARY OF DATA (CONT'D)

					AS	ASAI	ASMS	ASMSTS	TOTAL
SUDDEN DEATH	INCIDENCE IN CASES WITH KNOWN CAUSE OF DEATH (171)			No.	4	11	19	6	40
				%*	13.8	26.9	25.3	23.1	23.4
	AV. AGE SUDDEN DEATH			Yr.	70.2	54.4	52.1	33.5	52.0
	AV. AGE DEATH OTHER CAUSE			Yr.	63.2	54.1	49.2	37.5	50.8
	DEGREE OF STENOSIS			Av.	3.8	3.1	2.6	2.5	2.8
BLOOD PRESSURE				No.	28	60	88	27	203
				Av.	141/80	130/63	134/69	127/76	133/70
ELECTROCARDIOGRAM	455 CASES	CONDUCTION DEFECTS	LBBB	No.	7	24	5	0	36
				%*	6.7	12.5	3.8	0	7.9
			RBBB	No.	1	2	4	0	7
				%*	1.0	1.0	3.0	0	1.5
			INC. BBB OR I.V. BLOCK	No.	8	19	10	3	40
				%*	7.6	9.9	7.5	12.0	8.8
			A-V BLOCK	No.	9	27	19	5	60
				%*	8.6	14.1	14.3	20.0	13.2
		AURICULAR FIBRILLATION		No.	10	20	70	17	117
				%*	9.5	10.4	52.6	68.0	25.8
	127 CASES	LEFT VENTRICULAR HYPERTROPHY		No.	20	54	19	2	95
				%*	78	87.1	51.4	100	74.8
CALCIUM IN AORTIC VALVE	214 CASES	INCIDENCE		No.	18	38	32	3	91
				%*	62.1	59.4	34.8	10.4	42.5
	AV. AGE AT DEATH	WITH CALCIUM		Yr.	65.3	50.8	48.9	29.3	52.3
		WITHOUT CALCIUM		Yr.	65.5	47.6	43.3	37.3	44.5
	DEGREE OF STENOSIS	WITH CALCIUM		Av.	2.9	2.8	2.9	2.7	2.9
		WITHOUT CALCIUM		Av.	2.8	2.4	2.5	2.3	2.5
POST-MORTEM	188 CASES	DEGREE OF STENOSIS		No.	27	57	78	26	188
				Av.	2.9	2.8	2.7	2.5	2.7
	155 CASES	AVERAGE HEART WEIGHT		No.	27	36	71	21	155
				Gram	6'6	686	593	543	610

*Figures indicate per cent of total number of cases with this lesion, i.e., AS, ASAI, etc. See legend of Table I.

COMPLICATIONS AND SEQUELAE OF AORTIC STENOSIS

Patients with aortic stenosis are likely to develop one or more of the following complications: angina pectoris, syncopal attacks, congestive heart failure, myocardial infarction, and subacute bacterial endocarditis.

Congestive Heart Failure.—Criteria for estimating the onset of failure were a history of significant dyspnea, paroxysmal nocturnal dyspnea or ankle edema, or the finding of pulmonary râles, a large tender liver, or ankle edema on physical examination.

The fifty patients who developed subacute bacterial endocarditis were excluded from consideration in evaluating the data for congestive failure but will be considered at length separately. Furthermore, patients treated before 1930 were also excluded because it was about this time that mercurial diuretics were first used in about the same manner as employed at the present. It is our opinion that the introduction of the mercurial diuretic regimen definitely lengthened the life of cardiac patients after congestive symptoms first appeared. This, therefore, left 433 cases for analysis.

Among these 433 cases, there were 199 patients in whom congestive failure developed and the age at death was known. The average duration of life after the onset of symptoms of decompensation was 42.5 months. The average for thirty-seven cases of pure aortic stenosis was 22.7 months (1 week to 10 years). The combined average for seventy-one cases of aortic stenosis and insufficiency without mitral stenosis was 28.9 months (1 month to 17 years), while seventy-three cases having stenosis of both the aortic and mitral valves had an average of 56.4 months (1 month to 17 years). When stenosis of all three valves was present (18 cases) the average was 80.0 months (1 month to 18 years). It seemed quite clear that the duration of life after the onset of congestive heart failure was shortest in pure aortic stenosis, longest for those with trivalvular stenosis, and intermediary for those who had only aortic and mitral stenosis.

Since the percentage of patients with pure aortic stenosis having a past history of rheumatic fever was small, it was felt that the cases diagnosed as pure aortic stenosis might easily be separated into two distinct categories: those who had aortic stenosis due to rheumatic infection and those whose stenosis might have been due to degenerative processes. If this were true, then it was thought that patients with a past history of rheumatic fever might possibly develop failure and die at an earlier age than those in the degenerative group. In this regard there were five cases of pure aortic stenosis that had a past history of rheumatic fever that died at an average age of 63.2 years and fifty-eight patients without a rheumatic fever history with an average age at death of 65.8 years. Similar figures for aortic stenosis and insufficiency but without mitral stenosis showed that those with a rheumatic fever history died at an average age of 52.9 years (27 patients) and 52.6 years (57 patients) without a rheumatic fever history. It would appear that if these two groups were sharply different in etiology, there might have been a considerably greater difference between the ages at death. In fact, this lends support to the view that many of those that might have been called arteriosclerotic were also originally infectious or rheumatic.

In general, death from congestive heart failure was quite rare under 30 years and not very common under 40 years of age. In the aortic cases without mitral stenosis, the age at death was considerably lower if aortic insufficiency was present in addition to stenosis of the valve. The figures were 65 years for thirty-eight patients with pure aortic stenosis and 59 years for forty-eight with combined aortic stenosis and insufficiency.

In those patients who developed congestive failure, 173 had a past history of rheumatic fever. On the average, the first attack had occurred 31 years before the onset of failure, though there was a wide variation. The patient with pure aortic stenosis had had rheumatic fever on the average of 47.6 years before the onset of failure (range 26 to 72 years), while the aortic cases without mitral stenosis had had the initial attack 34.2 years previously. If both aortic and mitral stenosis were present the span was 28.2 years (range 2 to 56 years). With trivalvular stenosis, failure occurred 14.6 years following the attack of rheumatic fever (range 4 to 34 years). Therefore, patients with pure aortic stenosis not only had a history of acute rheumatic fever less frequently, but the interval between the initial attack and the onset of failure was considerably greater.

The following features of congestive heart failure were studied in the various subgroups of these cases: basal râles, hepatomegaly, pitting edema, and the history of paroxysmal nocturnal dyspnea. There did not appear to be any striking differences in the significance of the various evidences of heart failure as far as their prognostic values in the various subgroups. There were wide ranges in the duration of life after one or another of these features first appeared, i.e., rare cases carried on for ten to fifteen years after peripheral edema or an enlarged liver was first noted and even after paroxysmal nocturnal dyspnea first occurred. This was true whether the lesion was limited to the aortic valve alone or whether other valves were involved. To be sure, the duration of life was found to be strikingly different on the average in the various subgroups.

The relationship between auricular fibrillation and the progress of the disease was difficult to analyze in these cases because it was frequently impossible to tell when the arrhythmia first appeared. It was known that in at least nine of the cases, congestive failure was precipitated by the onset of this arrhythmia. Of the 177 cases in failure (excluding those who had subacute bacterial endocarditis) in whom electrocardiograms were taken, 112 showed auricular fibrillation. Of these, in forty-three cases the arrhythmia was known to have lasted more than one month, in nine less than one month, and in sixty the duration was unknown. However, one can say that in the presence of congestive failure, one-fifth of those who have only aortic involvement, two-thirds of those who also have mitral stenosis, and about three-fourths who have additional tricuspid stenosis will eventually develop auricular fibrillation. It is of some interest that when auricular fibrillation developed in cases of aortic stenosis without mitral stenosis, if hypertension was absent, the prognosis appeared to be quite grave, whereas if the pressure was elevated in such cases, the outlook was considerably better.

These observations were equally true when the analysis was limited to those cases that came to post-mortem examination. After excluding subacute bacterial

endocarditis, there were only seven out of 171 autopsied cases that never developed cardiac decompensation during life. Pathologic data regarding the severity of aortic stenosis in autopsied patients with congestive failure therefore did not differ significantly from the data on all the autopsied cases (Table II). On the whole, a moderately severe degree of aortic stenosis was present, represented by the figures 2.8 for aortic stenosis, 2.5 for mitral stenosis, and 1.7 for trivalvular stenosis.*

Angina Pectoris.—There were 159 patients definitely diagnosed as having angina, or 29.8 per cent of the total of 533 cases in this series. This very likely is an underestimate because the previous history of angina is not infrequently overlooked. When patients are troubled mainly with dyspnea, the anginal component not uncommonly disappears, and the patient fails to tell the physician that he had formerly experienced chest pain on effort.

The incidence of angina in cases of pure aortic stenosis was forty-eight of 131 cases (36.7 per cent) and in aortic stenosis and insufficiency seventy-eight of 224 patients (34.8 per cent). The figure for stenosis of both the aortic and mitral valves was thirty among 149 patients (20.8 per cent). If stenosis of all three valves was present, angina was still less frequent, three of twenty-nine cases (10.4 per cent). Thus angina occurred most frequently in stenosis of the aortic valve alone, less frequently when both the mitral and aortic valves were stenosed, and rarest with trivalvular stenosis.

About 65 per cent of the 159 patients with angina were males, whereas 60 per cent of all cases comprising this study were males. The men were predominantly normotensive (blood pressure below 150 mm. Hg systolic and 90 diastolic), but among the women just the opposite was true.

The average age at onset of angina and the range of ages varied considerably depending on the type of valvular lesion. In these 159 patients, the first symptoms were noted at an average age of 53.0 years, varying from 18 to 78 years. For pure aortic stenosis the average age at onset was 61 years (range 38 to 78 years). For other groups of aortic stenosis without mitral stenosis the average age at onset was 49.5 years (18 to 77 years). For stenosis of both the aortic and mitral valves the average was 49.3 years, (20 to 72 years) and for trivalvular stenosis 32 years (range 23 to 41 years). The decreasing age at onset of angina in the above groups corresponds to the decreasing average ages of the various groups as a whole, as the pure aortic cases were the oldest and the tricuspid cases, the youngest. What is significant is that angina is more frequent in pure aortic stenosis (36.7 per cent) and least in trivalvular stenosis (10.4 per cent) and intermediary in the cases with aortic and mitral stenosis (20.8 per cent).

Relationship of Aortic Insufficiency to Angina Pectoris.—It has often been assumed that aortic insufficiency per se with a low diastolic pressure is an important factor in the production of angina. This was based on the premise that the major portion of coronary flow occurs during diastole and that with a low

*The degree of stenosis as observed post mortem was indicated as follows: 1-slight, 2-moderate, 3-severe, 4-very severe.

diastolic pressure, perfusion of the coronary arteries would be decreased. Experience with free syphilitic aortic insufficiency in the past militated strongly against this concept. In this condition, there is practically no aortic stenosis accompanying the marked regurgitation, and yet anginal pain is extremely rare unless the coronary ostia are narrowed by the syphilitic aortitis. The analysis of cases in this study likewise appears to show that aortic insufficiency can play no important role in the production of anginal pain.

There were 131 cases of aortic stenosis without an aortic diastolic murmur of which forty-eight had angina (36.7 per cent). Similarly there were 144 cases of aortic stenosis with an accompanying aortic diastolic murmur and among these fifty-five had angina (38.3 per cent). It therefore follows that the presence of aortic insufficiency did not increase the incidence of angina in the presence of aortic stenosis. The factor of age was then investigated. In the group of cases between the ages of 50 and 65 years, there were fifty-two patients with pure aortic stenosis and 54 with additional aortic insufficiency. The average ages for these two groups were 56.9 and 55.3 years, respectively, and angina was present in 44.5 per cent of the former and 42.6 per cent of the latter. Here again there was no increase in the frequency of angina in those with aortic insufficiency when the average ages of the two groups were essentially the same. Although the number of cases in the age group 30 to 49 was too small to analyze statistically, here also there is no preponderance of angina among these with aortic insufficiency.

In estimating the prognosis of a patient with aortic stenosis after the onset of angina, data from all 159 cases in that category were studied. The age at death was not known for all of these cases, and in such instances the known duration of angina was used in the calculations. The total length of life after the onset of angina did not differ markedly for the various types of lesions. The general average was 4.1 years with a range of one week to 15 years. Twenty of the 159 cases or 12.6 per cent had angina for 10 years or more, and fifteen of the twenty did not have mitral stenosis. The age at onset in these fifteen cases ranged from 18 to 62 years (average 48 years), while that of the remaining five varied between 16 and 55 (average 42 years). The age at onset had some bearing on the duration of angina. The average duration of life from the initial onset of angina until death in forty-seven cases under 50 years of age was 5.6 years; whereas, in fifty-five cases over 50 years of age, this average duration was only 3.8 years. It is apparent that younger patients lived longer after the initial evidence of the anginal syndrome.

Of the fifty-two autopsied cases of angina pectoris, including subacute bacterial endocarditis, twenty-one were under 50 years of age and thirty-one were above 50 years of age. Of the twenty-one dying before 50, the coronary arteries of eighteen were described; coronary arteries were normal in five, had slight to moderate atherosclerosis without narrowing of lumen in ten, and severe sclerosis with or without narrowing in three, and no myocardial infarction either fresh or old in any. In the group of thirty-one above 50 years of age, the coronary arteries were described in twenty-eight, six were normal, nine had moderate atherosclerosis, and thirteen had severe atherosclerosis with or without narrow-

ing. In the latter group above 50, there were six cases with old or new myocardial infarction. The coronary arteries were described in only three of these six cases and all three showed severe atherosclerosis, calcification, and marked narrowing of the lumen, though no actual occlusion was demonstrated in any of the three. They were not examined by the Schlesinger technique of plastic injection, however, and some significant findings in the coronary arteries may have been overlooked. Thus the patients above 50 years of age gave evidence of much greater atherosclerosis and narrowing of the coronary arteries, as well as myocardial infarction. However, in both the younger and older groups, there was a significant number of cases (11) with angina pectoris who had essentially normal coronary arteries.

It was suspected that the degree of constriction of the valve would be greater in those suffering from angina than in those without an anginal component, and furthermore, that the stenosis would be most marked in patients with angina who showed no significant abnormalities in the coronary arteries. This did not prove to be true. The difference in the degree of stenosis did not appear to be very impressive between those with angina (3.0) as compared to those without angina (2.6). This slight difference was true throughout the various subgroups.

What was even more surprising was that the eleven patients who had aortic stenosis and angina pectoris but essentially normal coronaries had stenosis of only 2.2, while those with coronary artery disease and angina pectoris had stenosis of 3.3. It can be concluded that stenosis is not greater in those with angina.

In analyzing the weight of the heart in relation to angina, there appeared to be a more definite correlation. The average weight of the nine cases that had angina but showed no significant coronary sclerosis was 736 grams whereas the average age weight of those with angina and coronary sclerosis in thirty-seven cases was 618 grams. It seemed that considerable left ventricular hypertrophy may have been conducive to the development of anginal pain.

Syncope.—The incidence of syncope among cases of aortic stenosis depends on the care with which the history is taken. Clinically diagnosed cases were questioned specifically regarding that symptom, and the percentage of positive histories consequently was greater in that group. Males were more likely to have syncope, for while 60 per cent of the entire series (533 cases) were males, 75 per cent of those with syncope were males. Sixty-seven of the 533 patients (12.6 per cent) had a definite history of syncopal episodes, but the frequency varied considerably with the type of lesion. Cases with pure aortic stenosis had the highest incidence, 20.6 per cent, and the average for the other cases of aortic stenosis without mitral stenosis was 10.7 per cent. The general average for cases of bivalvular stenosis was 10.0 per cent. For stenosis of all three valves the incidence was lowest, 3.5 per cent. The frequency of the various lesions among those who had syncope was also analyzed. It was found that fifty-one (76 per cent) of the sixty-seven cases who had syncope had aortic stenosis without stenosis of the other valves. Fifteen (22.4 per cent) of these same sixty-seven cases had stenosis of both the aortic and mitral valves, and only one (1.5 per cent) had trivalvular stenosis. In a word, in the great majority the lesion was limited to the aortic valve.

The average length of life after the onset of syncope was determined in sixty cases, using either the age at death or the age last seen so that the figures given can be interpreted to be somewhat shorter than the true span. The general average was 3.3 years with very little variation for any of the subgroups. The average span for the pure aortic stenosis cases was 3.0 years with a range of a few days to 15 years. The range for the entire group also covered this same span, several days to 15 years.

One of the mechanisms that has been suggested as a possible explanation of syncope that occurs in aortic stenosis is a hypersensitive carotid sinus. This was only investigated in a selected number of cases, and it is impossible to analyze in detail the role of the carotid sinus in this regard. In only forty-three instances was the carotid sinus sensitivity tested and in none was true syncope produced. Twenty-seven of these had had syncope, and eleven showed a sensitive carotid sinus. Sixteen had no history of syncope, and of these, ten showed a sensitive carotid sinus. It follows that although carotid sinus sensitivity may be involved in some cases as a cause of syncope, it cannot explain the majority of such complications since the sinus is equally sensitive in both groups.

It is well known that disturbances in conduction are quite common in aortic stenosis. The possible role that this might have in the production of syncope was therefore analyzed. There were only fourteen of the sixty-seven cases with syncope who showed conduction abnormalities, i.e., auriculoventricular block, intraventricular block, or bundle branch block. This mechanism cannot be the important factor in the production of syncope. The same unimpressive results were obtained when the possible role of auricular flutter or of auricular fibrillation was analyzed in relation to syncope. There were eight of fifty-one cases of aortic stenosis without mitral stenosis who had auricular fibrillation and eleven out of sixteen with additional mitral stenosis who were fibrillators.

It seemed of some interest to determine whether those patients suffering syncope had any greater tendency to die suddenly. The mode of death was known in seventeen instances, and there were three sudden or instant deaths among these (17.6 per cent). The incidence of sudden death for the entire series was 18.8 per cent. It may be of some importance that all three had mitral stenosis as well as aortic stenosis. Among the fifty-one with lesions confined to the aortic valve who had syncope, none died suddenly. It would appear that syncope of itself does not indicate a likelihood of sudden unexpected death.

In most instances the explanation of the syncopal attacks remains uncertain because it is so rare for the physician to witness the episode. It is then difficult to be sure whether there has been a temporary asystole, some form of heart block, or a transient form of paroxysmal rapid heart action. The frequent association of the actual fainting spell with conditions that accelerate the heart such as physical effort or emotion makes one think that the state of unconsciousness results from temporary cerebral anoxia. A shortened diastolic filling accompanying accelerated heart action is particularly likely to decrease the cardiac output in cases of well-marked aortic stenosis. This may be the main mechanism in initiating syncope in these cases. It should be noted that in the sixteen cases examined post mortem, the degree of constriction of the aortic valve was 3.1

which is a significant degree of stenosis. The over-all average for the group was 2.8 so that the absence of syncope does not aid one in excluding severe aortic stenosis, but its presence will usually mean a high degree of constriction.

Sudden Death.—It is well known that sudden unexpected death is a fairly common occurrence in aortic valvular disease. The term sudden death is confined to those instances in which the patient, expected to live for days or weeks or much longer, dies instantly within a matter of seconds or a few minutes. If the terminal illness consisted of an attack of prolonged pain such as is seen in acute coronary thrombosis or in a state of shock or pulmonary edema lasting one-half hour or more, it was not included in this category of sudden death. Sudden death in those who had subacute bacterial endocarditis is also excluded. In this review, the mode of death was definitely known in 171 instances. There were forty so-called sudden deaths or 23.4 per cent. The number of sudden deaths in the various groups was as follows: four out of twenty-nine with pure aortic stenosis (14 per cent); eleven of forty-one with aortic stenosis without mitral stenosis (27 per cent); and twenty-five of 101 with aortic stenosis with mitral stenosis (25 per cent). It was somewhat surprising that there were so many instances of sudden death among cases of aortic stenosis that also had mitral stenosis. It even appeared to be a more frequent mode of exitus in the mitral group than in those who had only pure aortic stenosis. The average age at death of these forty patients dying suddenly was 52 years (range 17 to 85 years), while the average age at death of the remaining 131 cases was 50.8 years. The average age at the time of the sudden death for the various subgroups was as follows: pure aortic stenosis 70.2 years, other cases of aortic stenosis without mitral stenosis 54.4 years, aortic stenosis with mitral stenosis 52.1 years, and trivalvular stenosis 33.5 years. Comparable figures for the remaining 131 cases are pure aortic stenosis 63.2 years, other cases of aortic stenosis without mitral stenosis 54.1 years, aortic stenosis with mitral stenosis 49.2 years, and trivalvular stenosis 37.5 years. In other words, sudden death occurred during the later stages of the disease and not in the early, uncomplicated phase. It must be borne in mind that the material in this study is unduly weighted in favor of the more advanced cases who are disabled, particularly by dyspnea or congestive heart failure. In fact thirty-eight of the forty cases had signs of dyspnea or more advanced failure. Those who were in an ambulatory state and not confined were less likely to have been in the hospital and to have had a post-mortem examination performed.

It is of some interest to know what relationship there might be between the sudden death and the history of angina or syncope. There were only three cases of syncope among this series with sudden death. This observation would indicate that syncopal attacks do not predispose to sudden death. On the other hand, twelve of these patients had a definite history of angina pectoris, and in an additional six the history was too vague to be diagnostic. It is fair to say that more cases might have been detected if a careful deliberate inquiry had been made concerning anginal symptoms that might have been present, especially before dyspnea set in. Four of these twelve with angina were under 50 and the other eight over 50 years of age, (range 23 to 75 years). In any event, the incidence of twelve out of thirty-four (36 per cent) makes angina a fairly common precursor of sudden death in this condition.

The appearance of the coronary arteries was described in eleven of the twelve cases with angina pectoris. Among the eight of those over 50 years of age, sclerosis of varying degrees was found in all instances. Two of the three under 50 years of age showed normal coronary arteries, and in the third only slight sclerosis was detected. Of the remaining twenty-six cases of sudden death in which the condition of the coronary arteries was described, eleven were under 50 years of age, of which eight showed no coronary sclerosis and three slight to moderate sclerosis. Among the fifteen over 50 years of age, there were only two with no sclerosis, two with slight sclerosis, and eleven with moderate to advanced sclerosis. As would be expected, the absence of coronary sclerosis was more common in the younger patients. It is also in the younger group that many of those who had mitral stenosis in addition to aortic stenosis were to be found. It is evident that sudden death occurred not infrequently in the absence of significant coronary sclerosis.

Myocardial infarctions of varying ages were found in nine instances, all but one of which showed considerable coronary sclerosis. In the remaining one, the sclerotic process was slight. In no instance of sudden death in this series was a frank pulmonary embolus found to be the cause. It is of interest therefore that infarction of the heart muscle was not found to result from aortic stenosis per se, but required additional structural changes in the coronary vessels.

An estimate of the degree of stenosis was made in the forty cases that died suddenly. There were only four who had so-called pure aortic stenosis and the average degree of constriction among these was 3.8. This represents a much more severe stenosis than the general average, though the number of cases involved is obviously much too small for a reliable conclusion. The remaining cases with or without mitral stenosis showed about the same degree of aortic stenosis as was present in the entire study.

ELECTROCARDIOGRAPHIC FINDINGS

Electrocardiograms were studied in this group of patients from several points of view. The main feature that was investigated was the evidence of hypertrophy of either ventricle, particularly the left. In addition, the frequency of conduction defects and of auricular fibrillation was noted. For purposes of the latter two disturbances, the entire series of 533 cases was reviewed. The determination of ventricular hypertrophy was limited to those cases observed since 1946, when the more systematic electrocardiographic survey of the precordial leads was introduced. This afforded more definitive electrocardiographic data concerning hypertrophy of the two ventricles.

Electrocardiographic tracings were available in 455 of the total of 533 cases. Of these, 297 had aortic stenosis without mitral stenosis and 159 had aortic stenosis with mitral stenosis. Conduction defects which included either bundle branch block or some degree of auriculoventricular conduction delay were present in 120 (26 per cent) of the cases. This occurred somewhat more frequently in those with aortic stenosis without mitral stenosis. Left bundle branch block was found in thirty-six instances (8 per cent), thirty-one of which had aortic stenosis

without stenosis of other valves. In fact, it appeared to be most common in those cases of aortic stenosis who also had some insufficiency of the aortic valve. On the other hand, right bundle branch block was rare, occurring only in seven cases (1.5 per cent) four of which had stenosis of both the aortic and mitral valve. Incomplete bundle branch block or intraventricular block was present in forty cases (9 per cent). First, second, or third degree auriculoventricular block was present in forty-seven (10.3 per cent), two (0.4 per cent), and eleven (2.4 per cent), respectively. In some of these patients more than one type of auriculoventricular and/or intraventricular block existed simultaneously. It should be noted that a large number of these patients had been receiving digitalis. This could account for some of the instances of first degree auriculoventricular block, but from our experience it could not account for any of those with higher degrees of auriculoventricular block or bundle branch block.

It is well known that auricular fibrillation is a common accompaniment of mitral stenosis and compartively rare in aortic valve disease. In this series auricular fibrillation was found in 10 per cent (20 out of 297 cases) of those who had aortic stenosis without mitral stenosis, and in 55 per cent (87 out of 158 cases) of those who had aortic stenosis with mitral stenosis. It is of interest that some degree of hypertension was present in more than one-half of those with auricular fibrillation who had aortic stenosis without mitral stenosis. When the arrhythmia was known to have been present for a considerable time (more than one year), hypertension was particularly frequent, as it was present in eight out of ten such instances. The remainder of the twenty had had the arrhythmia only for several months or as a terminal event. In contrast, thirty-nine of the eighty-seven with fibrillation who had aortic stenosis with mitral stenosis had had this arrhythmia for several years and hypertension was present in only one-third of these thirty-nine. It follows from the above analysis that the presence of persistent auricular fibrillation in a case of aortic stenosis is suggestive evidence of accompanying mitral stenosis, especially in the absence of hypertension. Furthermore, when the arrhythmia is found in a case of aortic stenosis in which there is no evidence of mitral stenosis and hypertension is absent, the prognosis is likely to be grave. Such a patient will almost always succumb within weeks or a few months, whereas if hypertension is present with auricular fibrillation, the survival period may extend for a few years after the onset of the arrhythmia.

The most valuable information to be obtained from the electrocardiogram in relation to the diagnosis of aortic stenosis concerns the question of ventricular hypertrophy. One would expect the left ventricle to become hypertrophied after a sufficient time had elapsed if a significant degree of aortic stenosis were present. Contrariwise, as a result of mitral stenosis, hypertrophy of the right ventricle ought to occur in the course of time. From recent experience, it has appeared to many investigators that the electrocardiogram affords fairly reliable evidence of ventricular hypertrophy, and in fact appears to be more accurate than data obtained by roentgenologic examination. The following criteria for left ventricular hypertrophy in adults have been used, in the main, for this study: R_1 plus S_3 greater than 25 mm.; R_{aVL} 11 to 13 mm.; and SV_1 plus RV_5 or RV_6 greater than 35 mm., with or without typical changes in the S-T segment or T wave.[18]

In this analysis we attempted to have at least two of these criteria present to identify a tracing as indicative of left ventricular hypertrophy. Inasmuch as unipolar limb and precordial leads were not used in the early years in this hospital, the analysis was confined to 127 cases observed since 1946.

Of the 127 cases in which adequate electrocardiograms were available, there were eighty-eight with aortic stenosis without mitral stenosis and thirty-nine with combined aortic and mitral stenosis. Among the eighty-eight without mitral stenosis, seventy-four (84.1 per cent) showed evidence of left ventricular hypertrophy. Three had left bundle branch block, three had right bundle branch block, and there was one each of incomplete left and incomplete right bundle branch block (this last patient died from pulmonary insufficiency due to pulmonary fibrosis). Of the remaining six, three were designated as having left-axis deviation, and three were regarded as showing normal curves. The great rarity of electrocardiograms that failed to show left ventricular hypertrophy or some defect in bundle branch conduction was obviously very striking. This was true at least in the late stages of the disease. During the earlier years, however, there were some cases of definite aortic stenosis in which the electrocardiograms had not yet shown any evidence of ventricular hypertrophy. It is of interest that all of the fourteen cases that were examined post mortem had electrocardiographic evidence of left ventricular hypertrophy or some intraventricular conduction defect. In eleven of these fourteen cases, figures for the thickness of the left ventricular wall are available. The thickness of the left ventricular wall was greater than 20 mm. in nine of these and was 15 and 16 mm., respectively, in the other two. Whenever electrocardiographic evidence of left ventricular hypertrophy was found, there was likely to be a high degree of stenosis (Grade 3 or 4). This was true in eleven out of these fourteen autopsied cases. The remaining three had only Grade 1 stenosis. One of these had left ventricular hypertrophy by the electrocardiogram, and no measurement of the thickness of the left ventricle was available from the autopsy protocol. The second had a considerable degree of coexistent aortic insufficiency and had left ventricular hypertrophy by electrocardiogram and by post-mortem measurements. The third was the previously mentioned case with pulmonary disease and incomplete right bundle branch block; he had evidence of increased thickness of both the right and left ventricular walls at autopsy. It is of further interest that there is not a single instance of right ventricular hypertrophy by the electrocardiogram in the entire group of aortic stenosis without mitral stenosis. This was true despite the fact that at autopsy the average thickness of the right ventricular wall was 6.2 mm. Finally, the absence of electrocardiographic evidence of left ventricular hypertrophy in a case of aortic stenosis would indicate that the degree of constriction must be slight.

The electrocardiographic determination of hypertrophy when both ventricles are involved is not simple. At times it was possible to suspect from the curves that both ventricles were hypertrophied, and this prediction was occasionally confirmed at autopsy. There were other cases when post-mortem examination showed hypertrophy of both ventricles with well-marked stenosis of both the aortic and mitral valves, but the electrocardiogram failed to show any evidence

of hypertrophy. In the thirty-nine instances of combined aortic and mitral stenosis there were twenty-one with and eighteen without evidence of left ventricular hypertrophy (54 per cent and 46 per cent, respectively). Among the latter eighteen there were five with some degree of bundle branch block, (two with complete and one with incomplete right bundle branch block, one with complete and one with incomplete left bundle branch block). There were, however, a few cases (three) who showed right ventricular hypertrophy without left ventricular hypertrophy, and a few others (seven) whose electrocardiograms suggested combined hypertrophy. If the cases seen before 1946 are included, we found a total of at least six instances of a high degree of aortic stenosis (Grade 3 or 4) with mitral stenosis, in which the only evidence of right ventricular hypertrophy was detected in the electrocardiogram. It follows therefore that the electrocardiographic indication of right ventricular hypertrophy in a case of aortic stenosis means that mitral stenosis is almost certainly present. A high degree of aortic stenosis, however, is still compatible with such tracings. To be sure, these same cases are likely to have a severe degree of mitral stenosis as well. There was no good correlation between ventricular dominance by electrocardiograms and ventricular wall thickness as measured at post mortem in combined valve disease.

PHYSICAL FINDINGS

Blood Pressure.—Correlations were made between blood pressure levels and the degree of aortic stenosis. It might easily be thought that a high degree of aortic stenosis would be incompatible with a sharply elevated blood pressure. Furthermore, it has been taught that there is a characteristic narrowing of the pulse pressure in aortic stenosis. As will be seen by the discussion that follows, neither of these impressions appeared to be correct. In the group that was examined post mortem, there were 203 cases in which the blood pressure was recorded. The over-all average was 133/70 mm. Hg with ranges of systolic 85 to 240 and diastolic 0 to 165. When those with pure aortic stenosis were analyzed, the average was 141/80 mm. Hg in twenty-eight cases. The extremes in this regard were systolic from 92 to 240 mm. Hg and the diastolic from 50 to 165. There was a slight tendency for the pressures to be higher in those with a lesser degree of stenosis. The average reading for those with Grade 1 and 2 stenosis was 159/85 mm. Hg and for those with Grade 3 and 4 was 134/80. It is of some interest that among twenty-one cases with a high degree of aortic stenosis (Grade 3 to 4) without an aortic diastolic murmur, there were two instances in which the diastolic pressure was comparatively low, 50 and 60 mm. Hg, respectively. The reverse is also true, i.e., a distinctly elevated systolic pressure may occur with extreme stenosis. There were in fact three instances with systolic readings from 150 to 170 mm. Hg that showed Grade 4 stenosis. It was somewhat surprising that moderate hypertension and occasionally even marked hypertension were so frequent. Forty-seven per cent of cases with aortic stenosis without mitral stenosis (165 patients) had a reading greater than systolic 150 mm. Hg or diastolic greater than 90 or both. However, the average degree of hypertension for this group was mild, 159/95 mm. Hg. Corresponding in-

cidence of hypertension in those with mitral stenosis was 31 per cent and for those with tricuspid stenosis it was 21 per cent.

It is obvious that those cases with an accompanying diastolic murmur would have on the average a somewhat lower diastolic pressure. The average reading for this group was 130/63 mm. Hg (60 cases). The average for those with aortic stenosis combined with mitral stenosis was 134/69 mm. Hg (88 cases), and those with additional tricuspid stenosis 127/76 mm. Hg (27 cases).

Inasmuch as one would wonder whether there could be a high degree of aortic stenosis accompanied by clinical evidence of aortic incompetence and a low diastolic pressure, it is significant that there were four cases that showed this combination of findings. They all had an aortic diastolic murmur. Two were of Grade 3 stenosis and two were of Grade 4 stenosis, and the diastolic pressure ranged from 50 to 30 mm. Hg. The inference is that a low diastolic reading in the presence of aortic insufficiency is still compatible with severe aortic stenosis.

In the analysis of blood pressure determinations, the age factor must be considered. If the cases are divided into those over and under 50 years of age, the readings are 143/80 and 129/67 mm. Hg., respectively. This includes 353 cases from the post-mortem, x-ray, and clinical groups of aortic stenosis without mitral stenosis. The differences of 14 mm. Hg systolic and 13 mm. Hg diastolic readings were small but showed the tendency of the older age groups to have slightly higher pressures. In all these analyses, the data obtained from the so-called clinical or ambulatory patients seen in office practice were quite similar to those subsequently examined post mortem.

There has been a clinical impression that the pulse pressure is peculiarly narrow in cases with aortic stenosis. This probably was based on isolated instances in which it was strikingly true. However, it must be an exceptional phenomenon because when cases of pure aortic stenosis are analyzed in which hypertensive patients are eliminated (systolic of 150 and diastolic of 90) the average reading was 130/74 mm. Hg (42 cases).

In review, it appears that the level of the blood pressure is not helpful in the diagnosis of aortic stenosis or even in the estimation of the degree of constriction of the valve. The systolic pressure may be quite low or very high, although when the systolic level is comparatively low it is more likely to accompany a higher degree of stenosis than if it is elevated. Furthermore, a low diastolic pressure with signs of aortic insufficiency is not incompatible with a high degree of aortic stenosis.

Systolic Murmur of Aortic Stenosis.—The most valuable finding that leads the physician to consider the diagnosis of aortic stenosis is the presence of a systolic murmur at the base of the heart, particularly in the aortic area. In fact, a systolic murmur was heard in every case but one in this series. The interpretation of a systolic bruit therefore becomes very important. It is quite evident, however, that many basal systolic murmurs are heard in patients who do not have aortic stenosis. It is commonly associated with hypertension whether in heart failure or not and when the valves are normal. There is reason to believe that in many such cases the turbulence producing a murmur may

result from the dilatation of the aorta which is such a frequent accompaniment of hypertension. In that way the normal aortic aperture may be regarded as relatively stenosed compared to the size of ascending aorta. Congenital lesions, particularly pulmonic stenosis, often show a basal systolic murmur. There are other conditions such as anemia, and nervous and febrile states that commonly manifest systolic murmurs. In trying to appraise the significance of a systolic murmur, many factors therefore need to be considered.[19]

It has been useful in trying to interpret the cause of a systolic murmur to designate its intensity. The gradations that have been currently employed have been from 1 to 6.[15] This technique has merit in that one observer can compare his observations with another if the same nomenclature is employed. Furthermore, although systolic murmurs (Grade 1 and 2) are common in non-cardiac individuals and in fact in those who have very little evidence of any disease, patients with Grade 3 murmurs or louder will almost always have some major abnormality and generally be suffering from some type of cardiovascular disease.

An attempt was made in this study to correlate the loudness of the systolic murmur with the degree of constriction of the aortic valve. Although it is customary to associate the diagnosis of aortic stenosis with a loud systolic murmur heard best in the second right intercostal space or aortic area, it has become more and more apparent that such a murmur may be equally loud over the mid-precordium or at the apex. This is not surprising when it is appreciated that the aortic valve when visualized on fluoroscopic examination during life lies to the left of the fourth left parasternal line. In fact, there are occasions when the systolic murmur is louder at the apex even when post-mortem examination shows no mitral involvement, certainly, at least, no mitral stenosis or other significant mitral valve disease. One can always say under these circumstances that the mitral valve was incompetent during life and produced a jetlike regurgitation with systole. This is a mechanism which cannot be proved or disproved by findings in the dead atonic heart. The problem might be further elucidated in the future by correlating fluoroscopic examination concerning systolic expansile pulsation of the left auricle or pressure tracings obtained from the pulmonary capillaries or left auricle by cardiac catheter with autopsy studies. For the present, it is a matter of individual judgment as to whether an apical systolic murmur in a definite case of aortic stenosis is entirely transmitted from the aortic valve or is due to a concomitant mitral incompetency. In the differentiation, the character of the sound and whether it has the so-called "diamond-shaped" configuration in the phonocardiogram may be utilized.[20,21]

A factor that is often neglected in the interpretation of a basal systolic murmur and in fact of all murmurs and sounds is the thickness and depth of the chest itself. It is obvious that in a patient with marked emphysema or in those with obese or deep chests, murmurs that actually are loud at their site of origin may be a good deal fainter when elicited from the chest wall. Furthermore, the loudness of the murmur necessarily depends upon the vigor of myocardial contraction. During severe low-output failure when the patient's blood flow is reduced, a systolic murmur could well be quite faint and become much louder

with recovery of compensation. The actual heart rate is another factor to be considered. With a slower rate and a longer diastolic filling followed by a necessarily increased systolic output, the systolic murmur can be louder than when the heart cycle is shorter. These changes are frequently displayed in cases of auricular fibrillation.

In the detection and interpretation of aortic systolic murmurs, it is desirable to auscultate with the patient in both the flat and the upright position, particularly during a held expiration. The murmur's transmission to the carotid arteries in the neck is often used as added evidence to support the diagnosis of aortic stenosis. This we believe is only partially true. Other loud murmurs, systolic or diastolic in time, no matter what their origin, may also be audible in the neck.[22] However, the point of maxium intensity of the systolic murmur of aortic stenosis is likely to be nearer the carotid arteries than other murmurs, and it is logical to assume that the turbulence resulting from aortic stenosis extends peripherally along the aorta. One would, therefore, be expected to hear the aortic stenosis murmur a little more readily over the carotid arteries than other loud murmurs.

In this review, an analysis was made of the loudness of the systolic murmur in relation to the degree of stenosis, to the presence or absence of a diastolic murmur, to the level of the blood pressure, and the effect of congestive failure. The average intensity of the basal systolic murmur in aortic cases without mitral stenosis was 3.6. The presence or absence of hypertension had no effect on the intensity of the murmur. The figure for those with systolic pressure greater than 150 mm. Hg was Grade 3.7 intensity for pure aortic stenosis and Grade 3.6 for aortic stenosis with insufficiency; whereas the reading for those with systolic pressures under 150 mm. Hg was 3.5 and 3.7, respectively.

Among the twenty-seven cases that had pure aortic stenosis and were examined post mortem, the degree of constriction of the aortic valve was Grade 4 in ten cases, Grade 3 in ten, Grade 2 in four, and Grade 1 in three cases. The average intensity of the systolic murmur in these four groups was 1.9, 3.4, 2.2, and 2.7, respectively. Corresponding figures for the intensity of the murmur for cases of aortic stenosis with insufficiency were 2.9, 3.4, 3.0, and 4.1, respectively. There was a total of fifty-nine cases in this group with aortic insufficiency divided as follows: seventeen with Grade 4 stenosis, sixteen with Grade 3, sixteen with Grade 2, and ten with Grade 1. It appears from the above analysis that the murmur certainly is not louder with greater degrees of stenosis, for in those with the most marked constriction (Grade 4), there was the faintest intensity of the murmur (Grade 1.9). This may possibly be due to the fact that a large number of such patients were more gravely ill with a poorly functioning myocardium and congestive failure at the time of the examination.

These data were confined to patients who died and whose physical findings were obtained during the last stages of their illness. The situation might be quite different if comparisons could be made between the intensity of the murmur and the size of the valve orifice in the ambulatory patient. This information is not available at the present. However, when the clinical group of cases with aortic stenosis was analyzed, most of whom were ambulatory, the proportion of

those having Grade 5 and 6 murmurs was much greater than in those that were examined post mortem. There were six out of fifty-four such clinical cases of pure aortic stenosis and nine out of thirty-four with aortic stenosis and insufficiency, a total of fifteen out of seventy-eight. In contrast, there were four among the eighty-six similar cases who were examined post mortem. However, the presence of aortic insufficiency renders the systolic murmur somewhat louder, even with the same degree of constriction of the valve. This latter observation is not surprising because of the increased systolic output when there is also a diastolic reflux. It was also noted that the systolic murmur was often louder at the apex than at the base; in fact, this was true in 16 per cent of the entire group of aortic stenosis without mitral stenosis, and the same percent held in the autopsied cases in whom no mitral involvement was demonstrated by direct examination.

It seems pertinent to illustrate some of the vagaries of the manifestations of aortic stenosis by a few illustrative cases.

A man, 58 years of age, complained of breathlessness. He had had rheumatic fever at the age of eight. There was no history of hypertension or of coronary pain. On physical examination there was no hypertension but there was marked emphysema. The heart rhythm was regular, and no murmurs whatsoever could be heard either at the apex or at the base of the heart. The diagnosis of calcific aortic stenosis had already been made by the roentgenologist who on routine fluoroscopy of the chest had detected a calcified aortic valve. The diagnosis might have been suspected because of the regular rhythm, absence of hypertension or coronary symptoms, and the rheumatic history. After he recovered compensation and became ambulatory, he was again examined by fluoroscopy and the same calcified aortic valve was seen. He was seen again on two later occasions and not even a Grade 1 murmur could be elicited on the most careful auscultation. He died suddenly about two years after he was first seen. In this case, the marked emphysema probably accounted for the absence of any murmurs.

Another somewhat similar patient was seen over the course of 20 years. During most of this time he had a faint Grade 1 basal systolic murmur and at times a Grade 1 aortic diastolic murmur. Occasionally the basal systolic murmur was of Grade 2 intensity. He had an emphysematous chest with an increased anteroposterior diameter. Although a calcified aortic valve was seen fluoroscopically at the age of 45, he carried on very well for seven years, having a few attacks of mild pulmonary edema and died of pneumonia at the age of 52. On post-mortem examination, the heart weighed 900 grams, and the aortic valve was calcified and showed moderate stenosis.

Among the cases included in this study there were several in which the intensity of the systolic murmur was carefully noted during the period of decompensation and found to increase one or more gradations in intensity with recovery of compensation. In one instance, a Grade 1 systolic murmur became a Grade 4 as the patient improved.

When patients are followed for a great many years, one has the opportunity of observing the development of the classical sounds of aortic stenosis. It is obvious that when a loud Grade 5 or 6 systolic aortic murmur is detected in a man 50 or 60 years of age with a calcified aortic valve who had had rheumatic fever 40 years before, it must have required a great many years for the constriction to develop. The murmur could not have been that intense when the valve first became involved. It is reasonable to assume that in the very early stages only a Grade 1 basal murmur may have been present. At that time it would have been impossible for anyone to make the diagnosis of early aortic stenosis, as faint basal systolic murmurs occur so often without organic heart disease. We have all had the opportunity of observing this very progress in physical findings on numerous occasions. One patient was examined in 1925 at the age of 16 having had rheumatic fever six years before. She showed a Grade 1 apical and basal systolic murmur. She was followed for 20 years thereafter. During this time systolic and diastolic murmurs were noted to increase in the following fashion. In 1931, the systolic was 2 and the diastolic was 2, in 1937 the systolic was 3 and the diastolic 3, in 1945 the systolic was 4 and the diastolic was 3. A systolic thrill be-

came palpable for the first time in 1937. There were other instances in which similar progress of the systolic murmur was noted in the absence of any diastolic component.

The inference from the above experience is that aortic stenosis begins insidiously and that in its earlier stages the only abnormal sign will be a slight systolic murmur and that at this stage of its development the diagnosis will be difficult if not impossible to make.

Thrill.—The presence of a systolic thrill in the aortic area is generally looked upon as a fairly reliable sign of aortic stenosis. In former years it was even regarded as being a necessary finding to make the diagnosis. With increased experience it has become clear that the diagnosis can often be made without the presence of a thrill, just as it has to be made in the absence of a very loud murmur. One should reserve the term systolic thrill for a condition in which the palpable vibration over the upper chest wall lasts a significant length of time. In this way it should be distinguished from a momentary systolic impact. If this definition is adhered to, systolic thrills of aortic stenosis are only felt in the presence of loud systolic murmurs and will never be felt when the murmur is faint. The detection of a thrill will depend upon the care exercised in the examination, and whether it is felt for with the patient sitting upright during a held expiration. Examination of these cases was not carried out with equal expertness in all instances. However, it is of interest that a basal systolic thrill was detected in all but one of forty-nine instances of aortic stenosis without mitral stenosis in which the systolic murmur was of Grade 5 or 6 intensity. Countrariwise, a thrill was felt in only two out of fifteen cases in which the murmur was Grade 2 or less. Even these three exceptional instances may be inaccurate. More careful appraisal of these cases would probably have elicited a systolic thrill in the single exception of a Grade 6 murmur and would have calibrated the murmur as louder than Grade 2 when a thrill was felt. In the intermediary groups, thrills were felt in forty-five out of ninety-one of Grade 3 intensity and 128 out of 151 Grade 4 intensity. In general we can reiterate that the presence or absence of thrills go hand in hand with the loudness of the corresponding murmurs and furthermore that they are no better criteria of the degree of stenosis than are the murmurs themselves.

Aortic Second Sound.—The decreased intensity or absence of the second aortic sound is commonly regarded as one of the features of aortic stenosis. This finding was analyzed in the cases herein reviewed. Notations were made concerning the intensity of the second aortic sound in fifty-six out of a total of 130 cases of pure aortic stenosis, and in 114 out of 216 cases of aortic stenosis and insufficiency without mitral stenosis. In the first group, the second sound appeared to be normal or increased in nine and decreased or absent in forty-seven instances. In seventeen of the latter forty-seven the second sound was thought to be absent. Similar findings were obtained in the 114 cases of aortic stenosis and insufficiency without mitral stenosis. Here, there were thirty-two normal or increased second sounds and eighty-two decreased or absent. The degree of stenosis could obviously only be determined in those examined post mortem, and

it was found that those showing the highest degree of aortic constriction (Grade 3 to 4) were much more frequently associated with a decreased second sound than those with less stenosis (Grade 1 to 2). However, there were isolated cases in which the sound was absent with slight stenosis, and conversely, it could be increased even with a high degree of stenosis. In the latter, some degree of hypertension was likely to be present but not invariably so. In following the progress of some of these cases over the course of many years, it was not infrequently noted that the intensity of the aortic second sound gradually decreased as the leaflets became less and less mobile. In general, a decreased or absent aortic second sound is to be expected in pure aortic stenosis unless hypertension is present and is also a finding in the large majority of the cases when aortic insufficiency accompanies the aortic stenosis.

Apex Impulse and Pulse Pattern.—Two other features of the physical examination that are of some interest in the diagnosis of aortic stenosis are the character of the apex impulse and the type of peripheral pulse. An almost necessary result of aortic stenosis is hypertrophy of the left ventricle. The apex impulse becomes heaving or lifting in quality. This is often readily felt and gives the examiner the impression of left ventricular hypertrophy even when the apex is felt close to the nipple line. At times there may be very little evidence of enlargement of the cardiac silhouette on x-ray examination when there is concentric hypertrophy of the left ventricle but no dilatation of its cavity. Under these circumstances the lifting character of the apex impulse is a better index of left ventricular hypertrophy than the x-ray. These findings will not be evident in patients with emphysema or those with large chests.

The so-called plateau-pulse is commonly mentioned as a feature of aortic stenosis. In general, this has not been very helpful and is more often elicited or commented upon after the patient is known to have aortic stenosis than before. Although difficult to detect, there are times when the peculiar p'ateau quality of the radial pulse is sufficiently characteristic to call attention to the diagnosis of aortic stenosis. A graphic portrayal of the pulse wave by means of a direct puncture of the brachial artery and a manometer is a much more reliable method of determining the peculiar quality of the pulse. With this technique, the slow upstroke of the systolic pressure curve and the rapidity of the fall may reflect some measure of the degree of stenosis and the possible degree of insufficiency of the aortic valve.

Subactue Bacterial Endocarditis.—Proved instances of subacute bacterial endocarditis occurred in fifty of the 533 cases or 9.3 per cent (Table III). This does not reflect an accurate incidence of the infection during the life span of patients with aortic stenosis because of the artifical nature of the material studied here. A more valid estimate of the frequency of subacute bacterial endocarditis in aortic stenosis would be determined from the study of the autopsy material alone. Here it is found that forty-three out of 214 cases (20 per cent) examined post mortem showed evidence of subacute bacterial endocarditis. This figure is slightly less than the incidence of subacute bacterial endocarditis in rheumatic valvular disease in general as reported in the past by previous observers.[23] All

but eight of these cases were observed before the discovery of penicillin. Since the introduction of the antibiotics both prophylactically and therapeutically, it already appears that the frequency of subacute bacterial endocarditis as a cause of death in rheumatic heart disease will be strikingly diminished.

TABLE III. SUBACUTE BACTERIAL ENDOCARDITIS*

		AS	ASAI	ASMS	ASMSTS	TOTAL
INCIDENCE OF SBE	Number	0	23	17	3	43
	%	0	25	21	10	20
AVERAGE STENOSIS	With SBE	0	2.2	2.3	2.0	2.2
	Without SBE	0	3.0	2.7	2.7	2.8
LOCATION OF VEGETATIONS	Aortic	0	17	2	0	19
	Mitral	0	0	3	1	4
	Aortic-mitral	0	4	10	1	15
	Aortic-mitral tricuspid	0	2	0	0	2
	Aortic tricuspid	0	0	1	1	2
	Tricuspid-pulmonic	0	0	1	0	1

*43 cases out of total autopsy series (214 cases)

The occurrence of this infection in the various types of valvular lesions varied somewhat. Among the total number of those with aortic valve disease alone, 25 per cent had subacute bacterial endocarditis (23 out of 93), 21 per cent of those with aortic and mitral involvement, (17 out of 82), and 10 per cent of the trivalvular cases (3 out of 29). It was rarest in cases of aortic stenosis without insufficiency or other valve lesions, and in fact in those examined post mortem there was so such case. However, there were two instances of subacute bacterial endocarditis in cases clinically diagnosed as pure aortic stenosis and three that had no aortic diastolic murmur but did have mitral stenosis. It would seem that some aortic valvular insufficiency predisposes to the development of subacute bacterial endocarditis, and that pure stenosis is not very conducive to bacterial growth on the valve. Another possibility is that when patients with pure aortic stenosis develop subacute bacterial endocarditis the bacterial involvement of the valve may produce incompetency so that a diastolic murmur previously absent becomes apparent. The average age at onset was 41 years. The length of survival after the onset of endocarditis was difficult to estimate because of the insidious nature of the initial symptoms, but it was thought to vary between two weeks and 10 months with an average of about three and one-half months. The age at death was approximately 10 years younger than that found in cases of aortic stenosis without subacute bacterial endocarditis.

Thirty of this group of fifty patients (60 per cent) had a history of previous rheumatic fever, which on the average had occurred 18.7 years earlier. Some type of heart trouble had been known by forty-two patients (84 per cent) for an average of 10.7 years. In one instance, there was a 40-year history of a heart murmur while other patients were unaware of any cardiac abnormality until the diagnosis of bacterial endocarditis was made.

Electrocardiograms were done in forty of these patients. Auricular fibrillation was present in five cases, and four of these developed this arrhythmia after the onset of the subacute bacterial endocarditis, so that only one patient had auricular fibrillation preceding his infection. This is in accordance with our previous impression that subacute bacterial endocarditis is rare after established auricular fibrillation.

Pathologic examination was performed in forty-three of the fifty cases of subacute bacterial endocarditis. There was no case of pure aortic stenosis. Twenty-three (53 per cent) had aortic stenosis and insufficiency, while seventeen (40 per cent) had both aortic and mitral stenosis, and three (7 per cent) had trivalvular stenosis. The degree of stenosis of the aortic valve varied from slight to extreme but was somewhat less than was found in autopsied cases which did not develop subacute bacterial endocarditis. The average degree of stenosis was 2.2 for the aortic valve, 2.3 for the mitral valve, and 1.7 for the tricuspid valve in the three cases in which this valve was also involved, and 3.0, 2.7, and 2.7, respectively, for those without subacute bacterial endocarditis. It follows that there is less constriction of the valves in cases dying of subacute bacterial endocarditis than those who succumb to other causes.

Only five of the forty-three autopsied cases did not have vegetations of the aortic valve, though nineteen had them on one or more other valves in addition to the aortic. For the most part, if stenosis of the aortic valve alone was present, vegetations were found only on that valve. Furthermore, if the aortic valve is involved (aortic stenosis and insufficiency or aortic stenosis, insufficiency and mitral insufficiency) and there is no mitral stenosis, vegetations were invariably found on the aortic valve but occasionally on the mitral valve as well. In the presence of both aortic stenosis and mitral stenosis, vegetations were most commonly found on both of these valves. Inspection of the mitral and tricuspid valves often revealed a certain amount of roughening and thickening which were sequelae of the same rheumatic process that led to aortic stenosis, though no stenosis or insufficiency of those valves was present. Such valves were occasionally found to have on their surfaces the vegetations of subacute bacterial endocarditis. In two cases of pure aortic stenosis, vegetations were found on both the aortic and mitral valves, and two others on the tricuspid valves as well as the aortic valves. In one case of aortic stenosis and insufficiency and mitral stenosis and insufficiency the vegetations were found only on the tricuspid and pulmonic valves.

Most of the patients developed congestive failure some time during the course of the endocarditis. Eight of the fifty cases (16 per cent) had cardiac decompensation which preceded the clinically manifest endocarditis by a period of at least six months, the total duration of congestive failure averaging 3.9 years. Twenty-

five of the fifty (50 per cent) developed it after the apparent onset of subacute bacterial endocarditis, while the remaining seventeen (34 per cent) did not go into "frank" failure during their illness. Thus a bout of endocarditis was frequently a precipitating cause of congestive failure, but failure occasionally preceded the infection by a considerable interval.

Thirty-nine of the forty-three protocols included a description of the coronary arteries. In eighteen instances they were said to be normal, in thirteen there was slight to moderate atherosclerosis without other findings, while five cases showed more severe atherosclerosis with some narrowing of the arterial lumen. The latter five cases averaged 57 years of age, considerably above the over-all average of 41 years for the fifty subacute bacterial endocarditis cases, and might be expected to have more atherosclerosis than younger patients. Three of the forty-three cases showed occlusion of a coronary artery by an embolic vegetation of subacute bacterial endocarditis which produced myocardial infarction and death.

The heart size in males varied from 300 to 1,120 grams, (average 646 grams), and in females 300 to 700 grams, (average 416); the general average was 584 grams. Hearts of subacute bacterial endocarditis patients were therefore somewhat smaller than those of cases dying of other complications of aortic stenosis.

In summary, about one-tenth of the patients in the series developed subacute bacterial endocarditis, at an average age of 41 years. Although auricular fibrillation was not uncommon after subacute bacterial endocarditis developed, there was only one instance where the arrhythmia was known to have preceded the infection. Congestive failure often complicated the course of subacute bacterial endocarditis and in a small number preceded the development of the infection. At autopsy the degree of aortic stenosis was usually moderate. The vegetations were always present on the aortic valve in these cases if mitral stenosis was absent, and they were occasionally also found on the mitral valve in addition.

Mode of Death.—It seemed to be of some interest to analyze the various modes of death that occurred in these cases of aortic stenosis. Even though some of these cases were seen intimately in the hospital, no absolute deduction can be arrived at because there were others in whom only meager information could be obtained from the family or friends as to the course of events immediately preceding death. Furthermore, in many instances, more than one factor contributed to the eventual demise. Information concerning the type of death was available in 214 cases (Table IV). Among these, forty died suddenly (18.7 per cent). This group included only those patients who seemed viable and either dropped dead while ambulatory or while they were ill but apparently expected to live for some time. There were seventy-four patients that died with congestive heart failure (35 per cent). In this group there were some who had other complications such as pulmonary infarction but these did not seem to be of primary importance, although they may well have played a contributing role. There were nineteen cases of pneumonia (8.8 per cent), practically all occurring before the introduction of penicillin. In these the infection brought the course of the illness to a premature end. At the present time, such a complication could be

satisfactorily combated. Subacute bacterial endocarditis accounted for forty-three deaths (20.1 per cent). This type of death is now largely preventable. Death due to acute myocardial infarction occurred in five cases (2.3 per cent), from pulmonary emboli in ten cases (4.6 per cent), and from cerebrovascular accidents in nine cases (4.1 per cent). All of the above types of death account for approximately 94 per cent of the cases. Death in the remaining 6 per cent was due to miscellaneous causes such as cancer, cirrhosis of the liver, quinidine intoxication, etc.

TABLE IV. TYPE OF DEATH

	CHF	SBE	SUDDEN	PNEUMONIA	PULMONARY EMBOLI	CVA	MYOCARDIAL INFARCT.	MISC.	NON-CARDIAC	TOTAL
Number	74	43	40	19	10	9	5	6	8	214
Per cent	35	20.1	18.7	8.8	4.6	4.1	2.3	2.7	3.7	100.0

It is our judgment that when the valvular deformity is slight (less than Grade 2) a patient with aortic stenosis without mitral stenosis would not be expected to die of heart failure or if such failure is present, some other contributing cardiac disability such as coronary sclerosis would be found. In fact, there was only one instance in this series of Grade 1 pure aortic stenosis in which death occurred in congestive heart failure and there was no other important contributing cause noted although smoldering rheumatic carditis was suspected. Our conclusion from this is that when congestive heart failure is present in aortic stenosis and there is no other cause detectable, the degree of stenosis is very likely to be fairly marked.

The obvious inference from these data is that the overwhelming majority of cases of aortic stenosis die as a result of heart disease and its customary complications. Although it is difficult to draw accurate inferences because of the changing vital statistics during the past 50 years, it would appear that the normal duration of life is shortened somewhat in cases of pure aortic stenosis and considerably in those with additional valvular involvement.

Roentgenologic Consideration.—The most important finding on roentgen examination for the diagnosis of aortic stenosis is the detection of calcification of the valve on fluoroscopy. The method for the detection of the calcium has been well described by Sosman et al.[20a] The valve is generally most readily seen with patients in the right anterior oblique position, though occasionally the left anterior oblique is preferable. The relationship of calcium to other factors such as the degree of stenosis will be discussed elsewhere. There are other x-ray findings in cases of aortic stenosis that are less valuable but of some importance. Hypertrophy of the left ventricle is almost a constant finding. The left lower border of the cardiac silhouette takes on a rounded appearance and more often extends laterally than in a downward direction. The beat is only hyperactive when insufficiency of the valve is also present. The left auricle and main pulmonary artery are not prominent unless there are accompanying mitral lesions.

The ascending aorta is often moderately dilated giving an appearance of widening of the mediastinum. We suspect that pulsation of the aortic knob is likely to be decreased with pure aortic stenosis and probably increased when a sufficient degree of regurgitation is also present. The appearance of the cardiac silhouette is altered by additional lesions such as mitral or tricuspid stenosis, as one would predict, because of the dilatation and hypertrophy that would occur in the left auricle, pulmonary artery, and right side of the heart. In general, it is true that the left ventricular chamber is larger in aortic stenosis with insufficiency than without insufficiency. It is also quite striking that cases with pure aortic stenosis may have marked hypertrophy of the left ventricle as shown by post-mortem examination when the measured size of the heart on x-ray is only moderately enlarged. The cardiac silhouette, in fact, is often much greater in cases of mitral valve disease with or without aortic stenosis than in those with aortic stenosis alone, while the heart weight at autopsy is greater in those with aortic stenosis than in those with aortic and mitral stenosis. The reason for this discrepancy is the great dilatation of the auricles that takes place in the mitral group with a small left ventricle in contrast to the marked concentric hypertrophy of the left ventricle without corresponding dilatation of the chambers that occurs in pure aortic stenosis.

MISCELLANEOUS OBSERVATIONS

Calcification.—The 214 patients who were examined post mortem were studied to determine the relationship between calcification of the aortic valve and other factors in the course of the disease. Ninety-one patients or 42.5 per cent of this group had some degree of macroscopic calcification of the aortic valve. The incidence in pure aortic stenosis was 62.1 per cent, in aortic stenosis with insufficiency but without mitral stenosis it was 59.4 per cent, with an additional mitral stenosis it was 34.8 per cent, and with trivalvular stenosis it was 10.4 per cent. It must be appreciated that this decreasing incidence reflects in large measure the decreasing ages of the respective groups. The average age at death in pure aortic stenosis with calcium in the valve was 65.3 years (18 patients) and in those without calcium it was 65.5 years (11 patients). For aortic stenosis with insufficiency similar figures were 50.8 years (38 patients) and 47.6 years (26 patients); corresponding ages for those with an additional mitral stenosis were 48.9 years (32 patients) and 43.3 years (60 patients), respectively. The number of patients involved in the trivalvular group was too small to make any valid comparisons. By using the same two groups, a survey of the average degree of stenosis of the aortic valve was made. It was found to be slightly greater in those with than in those without calcium except in cases of pure aortic stenosis where there was no difference. As to the influence of calcification on the degree of insufficiency, no valid estimate could be made from this study.

Other random observations were made which are of some interest. The earliest age at which calcification was found in the aortic valve at autopsy for the four main subgroups was 39 years for pure aortic stenosis, 23 years for aortic stenosis with insufficiency, 27 years for those who also had mitral stenosis, and 20 years for trivalvular stenosis.

It would be expected that older patients would show more calcification of the valve than those of a younger age. This was borne out by an analysis of the 214 autopsied cases. Of these, there were 110 patients over 50 years of age of which 53 per cent showed calcium and 47 per cent did not. In 104 cases under 50, there were 34 per cent with and 66 per cent without calcium. It was of some interest to see whether those who had a calcified aortic valve with a past history of rheumatic fever died at a different age than those without such a past history. Among twenty-nine instances of calcified pure aortic stenosis identified at post mortem or by fluoroscopic examination there were five with a past history of rheumatic fever who died at an average age of 62.5 years and twenty-four without such a past history whose age at death was 65.3 years. The corresponding figures for the cases of aortic stenosis and insufficiency were 52.6 years (21 patients) and 55.4 years (48 patients), respectively. This three-year difference does not seem significant.

Another question that comes to mind is the frequency of calcification in those with and those without a past history of rheumatic fever. Among ninety-three cases of aortic stenosis without mitral stenosis there were thirty-two who had a rheumatic history and of these twenty-one showed calcification (69 per cent), and there were thirty-five (57 per cent) who showed calcification among sixty-one aortic cases without a rheumatic history. The percentage of calcified aortic valves was a good deal less when the mitral valve was also stenosed. Among 131 such cases, eighty had a past history of rheumatic fever and only fifteen showed calcium in the aortic valve (18.8 per cent). There were forty-one without such a past history and twenty-one (51.2 per cent) showed calcification. The reason for this high incidence was the fact that the age at death was 14 years greater in the latter group (54.4 years) than in the cases who did have a rheumatic history (40.2 years).

Identification of a calcified aortic valve by x-ray was made appreciably earlier in those with a rheumatic fever history. The average age at which calcium was seen in pure aortic stenosis was 55.7 years in seven patients with a rheumatic fever history and 65.6 years in 42 patients without this history. For aortic stenosis with insufficiency these figures were 49.4 years (31 patients) and 57.1 years (61 patients) and for additional mitral stenosis they were 45.6 years (23 patients) and 52.7 years (21 patients), respectively. It should be realized that these are ages at which the calcified valves happened to be seen and not the age at which they developed or might have been seen. The difference seems to be best explained by the fact that people with known rheumatic fever history are more likely to be seen earlier and examined by physicians and possibly by fluroscopy even when asymptomatic.

The average number of years after the last known attack of rheumatic fever at which calcium was seen was 47.1 years for pure aortic stenosis, 34.6 years for aortic stenosis with insufficiency, and 31.7 years for aortic stenosis with additional mitral stenosis.

Development of a calcified aortic valve visible by x-ray can occur at an early age regardless of the presence or absence of a rheumatic fever history. For pure aortic stenosis the earliest age at which a calcified aortic valve was seen with

rheumatic fever history was 43 years and without a rheumatic fever history was 41 years. When aortic insufficiency was also present, the ages were 29 years with a rheumatic history and 34 years without, and with bivalvular stenosis these ages were 28 and 38 years, respectively. The shortest interval after a known attack of rheumatic fever in which visible calcium was seen in the aortic valve by flouroscopy was 16 years in a patient with aortic and mitral stenosis. The obvious inference from these data is that calcification is a slow or gradual process and becomes visible only many years after the valve has first suffered its injury. This interval can be as short as 15 years but may also be as long as 50 years or more.

Basal Metabolic Rate.—It is common knowledge that congestive heart failure may be associated with an increase in the basal metabolic rate even when the thyroid gland is normal. Difficulties arise when cardiac patients actually have masked thyrotoxicosis. Here the metabolism is likewise elevated, but the hyperactive thyroid gland is the actual cause. The differentiation between these two groups at times may be very difficult. Some years ago attention was called to the fact that the basal metabolic rate may be elevated in some cases of aortic stenosis without congestive heart failure.[24] Further analysis of the question was made in a limited group of cases in this study. There were seventy-two instances in the entire series in which basal metabolic rates were determined. Among these there were twenty-nine in which the basal metabolic rate was over plus 20, with an average of plus 33.5, ranging from plus 20 to plus 55 per cent. In all of these twenty-nine cases the thyroid gland was examined at post mortem or after a thyroidectomy was performed. Twenty-seven of the twenty-nine showed normal glands and in the other two there was evidence of previous hyperactivity.

The inference from these observations is that a moderate elevation of the metabolic rate can be found in some cases of aortic stenosis with or without mitral stenosis that cannot be accounted for by the degree of dyspnea or by any pathology of the thyroid gland. In such cases, a diagnosis of additional thyrotoxicosis would have to depend on further clinical evidence and by the aid one could obtain from determining the radioactive iodine uptake and the protein-bound iodine.

Heart Weight.—A study was made of the average weight of the hearts at autopsy of 155 cases of aortic stenosis excluding those with subacute bacterial endocarditis and they were further analyzed for the effect of other factors such as the degree of constriction of the aortic valve, the blood pressure level, the duration of congestive heart failure, the age and sex, and the concomitant presence of other valve lesions.

The average weight for the 155 cases was 610 grams, ranging from 300 grams to 960 grams. For pure aortic stenosis the average was 606 grams (27 cases), for aortic stenosis and insufficiency without mitral stenosis it was 686 grams (36 cases), for those with an additional mitral stenosis it was 593 grams (71 cases), and for those with trivalvular stenosis it was 543 grams (21 cases).

The weight of the hearts of patients with aortic stenosis without mitral involvement showing the least degree of constriction (Grade 1 and 2) was less (590 grams in 18 patients) than in those with a Grade 3 and 4 stenosis (672 grams

in 44 patients). The difference was somewhat greater in those with aortic stenosis without insufficiency than in those with insufficiency. When mitral stenosis was also present, there was no significant difference in the heart weights with varying degrees of stenosis of the aortic valve. It is thought that the varying degrees of hypertrophy of the right ventricle in these latter cases combined with other factors accounted for this lack of correlation.

The level of the blood pressure appeared to have no influence on the average heart weight in cases of aortic stenosis without mitral stenosis. When the blood pressure was under 150/100 mm. Hg, the average weight was 639 grams in sixty-one patients, and when the pressure was over 150/100, it was 634 grams in twenty-one patients. When mitral stenosis was also present, corresponding figures for the normotensive and hypertensive individuals were 545 grams in seventy-eight patients and 625 grams in thirty-one patients. It follows that in this latter group, hypertension is accompanied by heavier hearts.

There was very little difference in the heart weight of those that died after less than one year of congestive heart failure as compared to those who survived for a longer period of time although there was a slight tendency to heavier hearts in aortic stenosis with accompanying mitral stenosis if the congestive failure had been present for more than one year.

The factor of age had a very slight effect on the average weights. Those under 50, in general, had hearts that averaged about 40 grams heavier than those over 50 years of age. A more definite discrepancy became apparent in comparing the two sexes. The average weight for males was 679 grams (90 patients) and that of females 539 grams (65 patients). This striking difference obtained whether the mitral valve was involved or not.

It is apparent from the above study that cases of aortic valvular disease have a marked degree of cardiac hypertrophy, mainly left ventricular. The weight of the heart is less in those with added mitral stenosis and least in those with aortic, mitral, and tricuspid involvement. The weight is somewhat greater when the aortic valve is incompetent as well as stenosed and is greater in males than in females, but is not significantly altered by the level of blood pressure, age, or duration of congestive heart failure.

SUMMARY AND CONCLUSIONS

Because of the present interest in the surgical treatment of aortic stenosis a detailed study was made of 533 such patients. These consisted of 214 examined post mortem, 158 diagnosed by the detection of a calcified aortic valve on fluoroscopy, and 161 as determined by customary clinical criteria. The patients were divided into four major groups, i.e., pure aortic stenosis (131 cases), aortic stenosis with insufficiency (224 cases), aortic and mitral stenosis with or without associated incompetence (149 cases), and stenosis of the aortic, mitral, and tricuspid valves with or without accompanying insufficiency (29 cases).

Evidence was presented to indicate that the vast majority of patients with aortic stenosis are primarily rheumatic in origin even when of the calcific type.

A past history of rheumatic fever was much more frequently obtained in those in whom mitral stenosis as well as aortic stenosis was present than in the group in which the aortic valve alone was involved.

Males predominated in the aortic cases, females in the cases of trivalvular stenosis, and the sex distribution was about the same in those with aortic and mitral stenosis.

The life expectancy and the age at death have been influenced by the recent improvement in the care of cardiac patients. The average age at death of 326 known fatal cases in this study was 52.2 years. For pure aortic stenosis the average age was 65.3 years, for aortic stenosis and insufficiency it was 52.5 years, for aortic and mitral stenosis 48.4 years, and for trivalvular stenosis 36.5 years.

The average duration of life after the onset of congestive failure was 42.5 months; 22.7 months for pure aortic stenosis; 28.9 months for aortic stenosis and insufficiency; 56.4 months for aortic and mitral stenosis; and 80.0 months for trivalvular stenosis. When a history of rheumatic fever was present, the interval between the attack and the onset of failure varied as follows: 47.6 years for pure aortic stenosis, 34.2 years for aortic stenosis and insufficiency, 28.2 years for aortic and mitral stenosis, and 14.6 years for aortic, mitral, and tricuspid stenosis.

Angina pectoris was present in 159 cases or 29.8 per cent of the entire 533 cases. The incidence was 36.7 per cent in pure aortic stenosis, 34.8 per cent in aortic stenosis and insufficiency, 20.8 per cent in stenosis of the aortic and mitral valves, and 10.4 per cent in those with trivalvular stenosis. The presence of aortic insufficiency was not found to increase the incidence of angina. The average duration of life after the onset of angina was about four years regardless of the different valves involved. Although the coronary arteries were significantly sclerosed in most cases with angina, there was a small number in the older age group and a larger number in the younger age group who had angina with essentially normal coronary vessels. The degree of aortic stenosis was not necessarily great in cases with angina with normal coronary arteries, although the weight of the heart was likely to be markedly increased in such cases.

Syncopal attacks occurred in at least 12.6 per cent of the series. The incidence was highest with pure aortic stenosis (20.6 per cent), 10.0 per cent in aortic and mitral stenosis, and was quite rare in the group with trivalvular stenosis, 3.5 per cent. The average duration of life after the onset of syncope was about three years and was much the same in the various groups. There generally was a high degree of stenosis of the aortic valve in these cases with syncope.

Sudden death occurred in forty instances (23.4 per cent) where the mode of death was known, excluding subacute bacterial endocarditis. The incidence was about the same whether mitral stenosis was present or not, and it occurred at the average age of 52 years. Syncope did not seem to predispose to sudden death, but there was a frequent (36 per cent) past history of angina. In the majority there was significant coronary sclerosis, but in ten the coronary arteries were essentially normal. The degree of stenosis of the aortic valve in these cases was no different from that of those who did not die suddenly.

Three electrocardiographic features were analyzed. Some form of conduction disturbance was present in 26 per cent of the 455 cases in whom tracings were available. Left bundle branch block was much more frequent when the aortic valve alone was involved than in those with additional mitral stenosis. There was no appreciable difference in the other forms of conduction disturbances. Auricular fibrillation was present in 10 per cent of those with aortic stenosis alone and in 55 per cent of those who also had mitral stenosis. When the blood pressure was normal in cases of auricular fibrillation with aortic stenosis but without mitral stenosis, the prognosis was grave, and it was definitely better if hypertension was also present. Among 127 patients in whom the electrocardiograms were adequate for the detection of left ventricular hypertrophy, it was found to be present in 74.8 per cent of the cases. In those with aortic stenosis without mitral stenosis, this figure was 84 per cent. The absence of left ventricular hypertrophy when the aortic valve alone was involved indicated only a slight degree of aortic stenosis. When mitral stenosis was also present, left ventricular hypertrophy was noted in only 51 per cent of the cases and its presence or absence did not reflect the degree of aortic stenosis.

The level of the blood pressure was not found to be helpful in the diagnosis of aortic stenosis. The average blood pressure for 203 cases examined post-mortem was 133/70 mm. Hg with a range of 85 mm. to 240 mm. systolic and zero to 165 mm. diastolic. Among those with pure aortic stenosis, the average was 141/80 mm. Hg with a range of 92 mm. to 240 mm. systolic and 50 mm. to 165 mm. diastolic. Although a very wide range of pressure readings was present, the lower systolic levels were more commonly obtained in those with a higher degree of stenosis and the lower diastolic levels in those with accompanying aortic insufficiency.

The most constant finding in these cases was the presence of a systolic murmur. This was generally loudest at or near the second right intercostal space, though in 16 per cent of the cases without mitral involvement it was actually louder at the apex. The average intensity of this basal systolic murmur was 3.6. The level of the blood pressure had no effect on the intensity of the systolic murmur. Congestive failure, however, definitely caused the murmur to decrease and with the recovery of compensation, the murmur grew louder. The intensity of the murmur bore no linear relationship to the degree of constriction of the valve. It would appear though that in the absence of aortic insufficiency or congestive failure, the murmur was loudest with moderate stenosis and less loud with slight or marked stenosis.

The presence or absence of a systolic thrill was directly related to the loudness of the murmur. It was practically never palpable unless the murmur was of Grade 3 and generally of Grade 4 intensity or louder.

The aortic second sound was decreased or absent in the majority of the cases of aortic stenosis without mitral stenosis but there were numerous instances in which the sound was normal or increased, especially if hypertension were present.

A forceful or lifting apex impulse proved to be a valuable indication of left ventricular hypertrophy. The detection of a plateau pulse is difficult, though with care and training, it may be a helpful sign in some cases.

Subacute bacterial endocarditis was found in 10 per cent of this series. The clinical and pathologic findings in these cases were discussed. Vegetations were always found on the aortic valve when mitral stenosis was absent.

The mode of death was analyzed in 214 fatal cases. Forty cases (18.7 per cent) died instantly; seventy-four (35 per cent) of congestive failure; nineteen (8.8 per cent) of pneumonia; forty-three (20.1 per cent) of subacute bacterial endocarditis; five (2.3 per cent) of myocardial infarction; ten (4.6 per cent) of pulmonary emboli; nine (4.2 per cent) of cerebrovascular accidents; and fourteen cases (6.4 per cent) died of miscellaneous causes.

The most valuable roentgenologic finding was the detection of a calcified aortic valve. The frequency with which it is detected will depend upon the care and the experience of the fluoroscopist. The degree of stenosis was only slightly greater when the valve was calcified than when it was not. Although aortic stenosis must be present for years before the development of calcification, which is a slow process, a calcified valve may be detected in the third or fourth decade.

A moderate elevation of the basal metabolic rate (average plus 33.5 per cent) was found in twenty-nine of the seventy-two patients in whom this test was performed. In only two of these cases did the gland show any evidence of hyperactivity.

The average heart weight was 606 grams for pure aortic stenosis, 686 grams for aortic stenosis and insufficiency, 593 grams for aortic and mitral stenosis, and 543 grams for trivalvular stenosis. The weight of the heart was definitely greater in males than in females, greater in younger than in older patients, but was little influenced by the level of the blood pressure or the presence of congestive failure.

In general, it can be concluded that the diagnosis of aortic stenosis can be made with a high degree of accuracy. Considerable variation was found in the clinical progress of the disease. Finally, a prediction of the degree of stenosis could be made with only a moderate degree of accuracy.

REFERENCES

1. Christian, H. A.: Aortic Stenosis With Calcification of the Cusps, J. A. M. A. **97**:158, 1931.
2. Margolies, H. M., Ziellessen, F. O., and Barnes, A. R.: Calcareous Aortic Valvular Disease, Am. Heart J. **6**:349, 1931.
3. McGinn, S., and White, P. D.: Clinical Observations in Aortic Stenosis, Am. J. M. Sc. **188**:1, 1934.
4. Boas, E. P.: Aortic Stenosis, Angina Pectoris, and Heart Block as Symptoms of Calcareous Stenosis, Am. J. M. Sc. **90**:376, 1935.
5. Contratto, A. W., and Levine, S. A.: Aortic Stenosis With Special Reference to Angina Pectoris and Syncope, Ann. Int. Med. **10**:1636, 1937.
6. Marvin, H. M., and Sullivan, A. G.: Clinical Observations Upon Syncope and Sudden Death in Aortic Stenosis, Am. Heart J. **10**:705, 1935.
7. Clawson, B. J., Noble, J. F., and Lufkin, N. H.: The Calcified Nodular Deformity of the Aortic Valve, Am. Heart J. **15**:58, 1938.
8. Friedberg, C. K., and Sohval, A. R.: Nonrheumatic Calcific Aortic Stenosis, Am. Heart J. **17**:452, 1939.
9. Gross, L.: So-called Congenital Bicuspid Aortic Valve, Arch. Path. **23**:350, 1937.

10. Dry, T. J., and Williams, F. A.: Calcareous Disease; 228 Cases, AM. HEART J. **17**:138, 1939.
11. Karsner, H. T., and Koletsky, S.: Calcific Sclerosis of the Aortic Valve, Tr. A. Am. Physicians **55**:188, 1940.
12. Krump, C. W., and Bean, W. B.: Aortic Stenosis: A Study of the Clinical and Pathological Aspects of 107 Proved Cases, Medicine **27**:139, 1948.
13. Kiloh, G. A.: Pure Aortic Stenosis, Brit. Heart J. **12**:33, 1950.
14. Lewes, D.: Diagnosis of Aortic Stenosis, British Med. J. **1**:211, 1951.
15. Larzelere, H. B., and Bailey, C. P.: Aortic Commissurotomy, J. Thoracic Surg. **26**:31, 1953.
16. Bailey, C. P., Bolton, H. E., Jamison, W. L., and Larzelere, H. B.: Commissurotomy for Rheumatic Aortic Stenosis, Circulation **9**:22, 1954.
17. Dammin, G. J.: Personal communication.
18. Sokolow, M., and Lyon, T. P.: The Ventricular Complex in Left Ventricular Hypertrophy as Obtained by Unipolar Precordial and Limb Leads, AM. HEART J. **37**:161, 1949.
19. Freeman, A. R., and Levine, S. A.: The Clinical Significance of the Systolic Murmur, Ann. Int. Med. **6**:1371, 1933.
20. Levine, S. A., and Harvey, W. P.: Further Notes on Auscultation of the Heart, Proc. New England Heart Assoc., 1948-49.
20a. Sosman, M. C.: The Technique for Locating and Identifying Pericardial and Intracardiac Calcification, Am. J. Roentgenol. **50**:461, 1943.
21. Leatham, A.: The Phonocardiogram of Aortic Stenosis, British Heart J. **13**:153, 1951.
22. Levine, S. A., and Likoff, W. B.: Some Notes on the Transmission of Heart Murmurs, Ann. Int. Med. **21**:298, 1944.
23. Laws, C. L., and Levine, S. A.: Clinical Notes on Rheumatic Heart Disease With Special Reference to the Cause of Death, Am. J. M. Sc. **186**:833, 1933.
24. Smith, J. A., and Levine, S. A.: Aortic Stenosis With Elevated Metabolic Rate Simulating Hyperthyroidism, Arch. Int. Med. **80**:265, 1947.

THE AXOSTAT

II. Tests of Underlying Physical Principles and Results of Preliminary Clinical Applications

Robert C. Little, M.D., Daniel A. Brody, M.D., and Hall S. Tacket, M.D.

Memphis, Tenn.

In a preceding paper[1] a new electrocardiographic instrument, the axostat, was described which produced any desired number of interpolated leads between the conventional bipolar extremity leads. It was shown that axostat leads are equivalent to the projection of the spatial vectorcardiogram on any axis of the Burger or Einthoven triangles. It was emphasized that axostat leads do not contain any information that is not inherently present in the conventional Einthoven leads. However, axostat leads provide a number of "views" of the spatial vectorcardiogram which are not afforded by the conventional extremity leads, and therefore the hope was expressed that some of the axostat lead positions might prove superior to the present extremity leads for the purpose of demonstrating certain electrocardiographic abnormalities.

Other applications of the instrument suggest themselves. Such applications are related to the ability of the instrument to record transition-point electrocardiograms.* The angular position control of the device may be rotated until the transitional form of the electrocardiogram is obtained. In accordance with the principles demonstrated by Graettinger and his associates,[2] the addition or subtraction of 90° to the angular position at which the transitional form occurs gives the direction of the mean vector of the complex or wave. By employing a back electrode, the same information may be obtained for another plane of the Wilson tetrahedron.[3] Such knowledge of the direction of the projections of the mean spatial vector on two planes of the tetrahedron should determine the orientation of the mean spatial vector itself. Later in this paper formulas, derived by us, will be presented for calculating the orientation of mean spatial vectors from data of this nature. As will be shown, this type of computation greatly reduces the labor involved in determining the magnitude of mean spatial vectors and ventricular gradients.

From the Department of Medicine, University of Tennessee, Memphis, Tenn.

Supported by grants from the National Heart Institute, United States Public Health Service, and from the Memphis Heart Association.

Received for publication Feb. 24, 1954.

*Electrocardiograms in which the algebraic area under a particular wave or complex is zero.

Still another application of the axostat stems from the fact that the angular positions of transition-point electrocardiograms are at right angles to the direction of the mean vectors. Thus, transition-point electrocardiograms, as obtained with the instrument, should be exceptionally sensitive in recording the electrocardiographic changes due to various factors, particularly those which are essentially rotatory in nature.

RESULTS

Demonstration of Underlying Physical Principles.—Before applying the instrument to clinical material, the underlying principles were tested and confirmed by a series of experiments performed on an accurately calibrated electrical model. The model consisted of three resistors connected together in a delta. Two terminals of the delta, chosen at random, were connected in series with a relatively large variable resistor, a 22 ½-volt battery and an electrical key. One of the terminals of the delta, also chosen at random, was held at zero potential by grounding it. The three terminals of the delta were then connected at random to the lead wires of the axostat. Two components of the model were fixed resistors of 0.768 ohm each. The third component was a plug-box resistor which varied in nominal steps of 0.1 ohm between 0.1 to 50 ohms. In all cases the resistances were measured to four significant places by means of a precision Kelvin double bridge. Depressing and then quickly releasing the electrical key produced square-wave impulses at the terminals of the model. The variable resistor of the model was adjusted so that the square-wave potential difference between two of the terminals of the model was approximately 1 mv. This potential difference was then accurately determined by comparing it on the electrocardiograph* with the 1 mv.-calibrating signal. From this information and the known-resistor values of the model, the instantaneous potential at each terminal of the model was calculated to two decimal places.

In the first experiment the potentiometer control of the axostat was rotated to such a position that the square-wave failed to cause a deflection of the electrocardiograph stylus. According to the axostat theory this angular position, as read from the master dial, should be at right angles to the direction of the manifest potential produced by the model. The potentiometer control was then rotated through a 90° reading on the master dial in the direction which caused positive square-wave deflections. In this new position, which corresponded to an axis of registration having the same direction as the manifest potential, a series of square waves was recorded and their amplitude measured as accurately as possible. The direction and magnitude of the manifest potentials determined experimentally in four cases are compared in Table I with the calculated values. The differences between observed and calculated values do not exceed the experimental error. In some instances, the differences between the angular values were somewhat less than appears in Table I because fractions of a degree on the master dial were not read.

*Model EK-2, Burdick Corporation, Milton, Wis.

TABLE I. MANIFEST POTENTIALS OF AN ELECTRICAL MODEL AS DETERMINED BY THE AXOSTAT, COMPARED TO VALUES CALCULATED DIRECTLY FROM THE LEAD DATA

CASE	LEAD POTENTIALS (MV.)	MANIFEST POTENTIALS			
		AXOSTAT		CALCULATED	
		MAGNITUDE (MV.)	ANGLE (DEGREES)	MAGNITUDE (MV.)	ANGLE (DEGREES)
1	$E_1 = 1.06$ $E_2 = 1.20$ $E_3 = 0.14$	1.30	37	1.31	37¼
2	$E_1 = 0.77$ $E_2 = 1.78$ $E_3 = 1.01$	1.45	75	1.43	74½
3	$E_1 = 0.82$ $E_2 = 0$ $E_3 = 0.82$	0.97	−30	0.95	−30
4	$E_1 = 0.71$ $E_2 = 1.08$ $E_3 = 0.37$	1.14	50	1.11	49¾

In a second experiment, axostat leads were recorded from the model for each 10° position of the potentiometer. Tracings obtained in this fashion should represent the projection of the manifest potential of the model upon successive axes 10° apart. If this is correct, the amplitudes of the leads plotted in polar coordinates, should result in a circular figure. Inspection of Fig. 1 indicates that the axostat satisfactorily fulfills this condition.

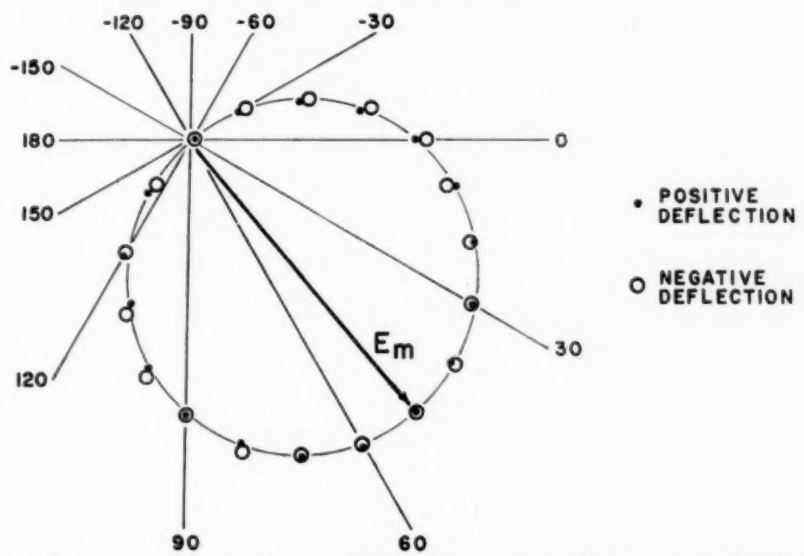


Fig. 1.—Polar coordinate plot of potentials recorded by the axostat from an electrical model for angular position settings 10° apart. E_m represents the manifest potential of the model. Further description in text.

Clinical Application.—The procedure for determining the direction of the manifest potential of the electrical model can also be used to find the direction of a mean cardiac vector. The only modification is that instead of rotating the potentiometer until the *absolute* area under the square wave is zero, the potentiometer is rotated until the *algebraic* area under a particular deflection is zero. Since the angular position at which this occurs is the transition point, the direction of the mean vector of the electrocardiographic deflection may be determined by adding or subtracting 90° to the reading on the master dial.

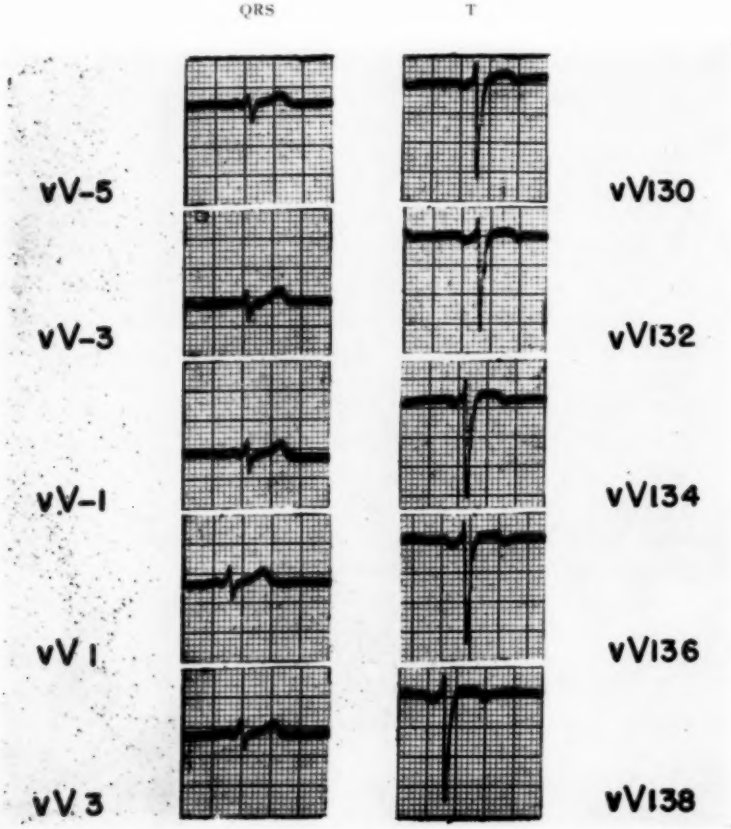


Fig. 2.—Illustration of the determination of transition points by means of the axostat. The center panel of each column shows the transitional form of the QRS complex and T wave, respectively. Departures from the transitional forms are seen as the angular position setting is varied in 2°-steps to either side of the transition points. Further description in text.

The precision with which the axostat accomplishes determinations of this type is shown in Fig. 2. The center tracing in each column is the transitional form of the QRS complex and T wave, respectively, of an experimental subject. To each side of the transition-point electrocardiograms are two tracings made in steps of 2° from the transitional position. In the first step slight, but fairly definite, departures from the transitional form are seen. In the second step the deviations from the transitional configurations are readily apparent. Therefore, in this case the transition points, and hence the directions of the mean vectors, were determined with an accuracy of at least ± 2°.

The exceptional sensitivity with which transition-point electrocardiograms record changes due to essentially rotatory influences is demonstrated in Fig. 3. In the left column of this figure are seen the conventional Einthoven leads and the transitional T lead (in this case vV-28°) of an experimental subject taken during shallow respirations. In the right column of the figure are the same leads taken at the end of a deep expiratory effort. As anticipated, the resultant T-wave changes are decidedly more marked in Lead vV-28° than in Leads I, II, and III.

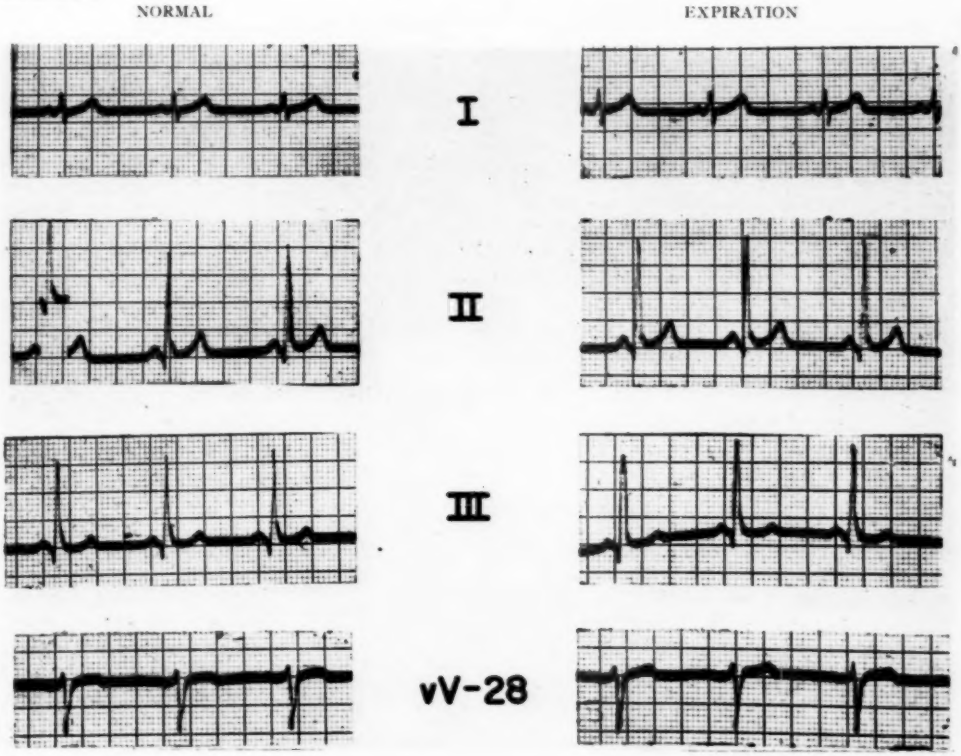


Fig. 3.—Illustration of the exceptional sensitivity of transitional forms of the electrocardiogram to essentially rotatory influences. Description in text.

An interesting and theoretically important relationship exists between the conventional Einthoven leads and axostat leads recorded at the angular positions of 0°, 60°, and 120°. According to the underlying theory of the instrument, Leads I, II, and III should be identical, respectively, to the tracings vV0°, vV60° and vV120°. This anticipated equivalence is demonstrated in Fig. 4. The particular significance of this observation is that these three special axostat leads, which are "unipolar" to the extent that they represent an elaboration of Wilson's theory of unipolar extremity leads,[4] are indistinguishable from the conventional bipolar extremity leads. On this basis, the bipolar leads would appear to be of the same class as unipolar leads, and therefore not necessarily inferior to unipolar leads.

Some types of electrocardiographic analysis require a knowledge of the direction of mean spatial vectors. Determinations of this type usually demand a great deal of laborious and questionably accurate planimetry. We have developed a method for accomplishing such determinations with the axostat without the need for measuring the area under electrocardiographic waves and complexes.

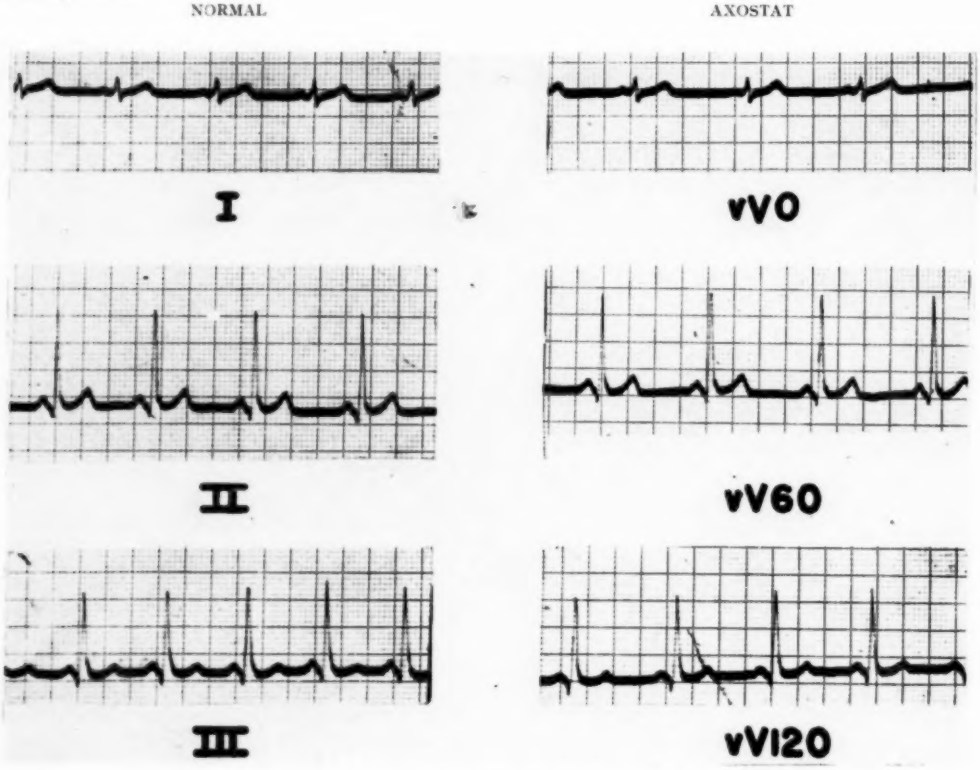


Fig. 4.—Illustration of the identity between the conventional Einthoven leads and the special axostat leads, vV0°, vV60° and vV120°.

The method for determining the direction of the frontal plane projection of the mean spatial vector has already been described. By means of a back electrode and a switching arrangement in the instrument the direction of the projection of the mean spatial vector on the BRF plane of the Wilson tetrahedron may also be determined in the same manner. From these data the direction of the projection of the mean spatial vector on the sagittal plane may be calculated from the formula

$$\cot \beta = \frac{\sqrt{6}}{2}\left[\frac{\sqrt{3}}{3} - \frac{\sin(\alpha + 30^\circ)}{\sin \alpha}\,\frac{\sin(\gamma + 30^\circ)}{\sin(\gamma - 30^\circ)}\right]$$

where β is the angular direction of the projection on the sagittal plane as measured clockwise from a horizontal line, α is the direction of the frontal plane projection, and γ is the direction of the projection on the BRF plane as measured clockwise from the line BR. The direction of the mean spatial vector is thus fixed in terms of conventional notation.

In the event that the frontal projection is directed at an angle of 150°, the direction of the BRF plane projection should be 30°. In this case the above formula will contain the indeterminate form 0/0. Nevertheless the orientation of the mean spatial vector may still be determined by measuring the direction of the projection in the LRB plane of the tetrahedron. The desired information may then be calculated from the formula

$$\cot \beta = -\frac{3\sqrt{2}}{4}\left[\frac{\cot \alpha}{\cot \delta} + \frac{1}{3}\right]$$

where δ is the angular direction of the projection in the LRB plane as measured clockwise from the line LR.

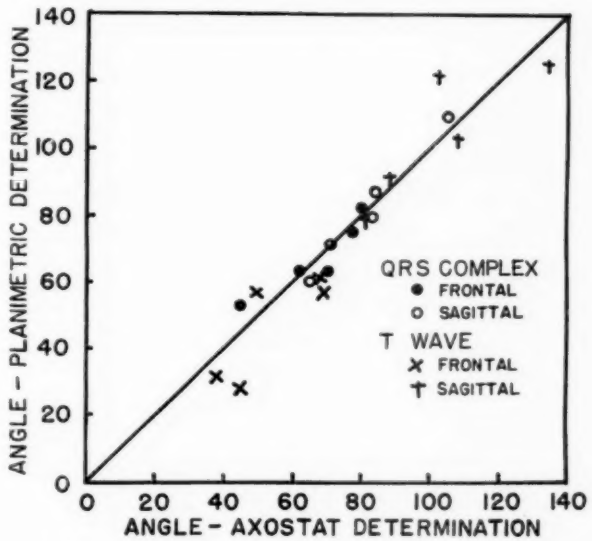


Fig. 5.—Illustration of the correlation between the axostat and planimetric methods of determining the orientation of the projections of mean vectors on the frontal and sagittal planes of the Wilson tetrahedron.

The theoretical developments outlined above were tested in five subjects by determining the spatial orientation of their mean QRS and T vectors with the axostat. The same information was also determined by the conventional method of measuring areas and plotting out the area data. Fig. 5 indicates that there was a good degree of correlation between the determinations as made by the two different methods. Although the formulas which we employed appear rather formidable, facility in their use is quickly gained. The axostat method of determining the orientation of mean spatial vectors has proved considerably less laborious than the conventional method.

DISCUSSION

The idea of an instrument which rotates the vector loop with respect to the "viewing" device is not a new one. Schmitt[5] has enunciated the principles for accomplishing this purpose by means of sine and cosine potentiometers. Schmitt

and Levine[6] and Milnor and his associates[7] have published descriptions of instruments which rotate the spatial vector loops in any desired direction. Since Milnor's instrument records a scalar electrocardiogram as well as the vectorcardiogram, it performs very much the same function as the axostat except for the differences in the lead connections. However, instruments based on Schmitt's principle appear to be unwieldy, complicated, and expensive, and it is doubtful that they will ever come into general use in clinical electrocardiography. On the other hand the axostat is relatively compact and inexpensive, and it is likely that its operation can be further simplified. Therefore, if experimental evaluation should prove that the axostat possesses any considerable merit, it could become readily available for general clinical use.

A basic defect of vectorcardiography, which was recently emphasized by Burch and associates,[8] is its inherent failure to delineate accurately the time relationships of the electrical cycle of the heart. Electrocardiography of the type produced by the axostat and similar instruments may therefore eventually prove to be a satisfactory compromise between standard electrocardiography and vectorcardiography because such electrocardiograms not only provide a great number of views of the vector loop but also preserve the time relationships.

The precision with which the axostat determines the position of a transition point (and hence the direction of a mean vector) depends not only upon instrumental factors but also upon the shape of the vector loop. When the vector loop is of the usual long, narrow configuration, the transition point can be determined with the precision depicted in Fig. 2. However, when the vector loop is circular or cardioid in shape, some of this precision is lost. Furthermore, in certain electrocardiographic abnormalities such as right bundle branch block of the so-called S type the transition point is difficult to determine on the basis of visual inspection alone. Further experience with the axostat may demonstrate the desirability of incorporating some sort of area-integrating circuit such as that described by Johnston and associates[9] in order to determine accurately the transition points of unusual wave forms.

It is too early in the development and application of the instrument to draw any conclusions as to its ultimate value in electrocardiography. There seems to be little doubt, however, that it will prove a useful tool at the investigative level. Its eventual usefulness in clinical applications remains to be demonstrated.

SUMMARY

1. The axostat is a relatively simple instrument for rotating vector loops with respect to the "viewing" device.

2. Experiments on an electrical model confirm the correctness of the underlying physical principles of the instrument.

3. Methods are described whereby the axostat may be employed to determine the orientation of mean spatial vectors without the necessity of measuring the areas under electrocardiographic waves and complexes.

4. The exceptional sensitivity of transition-point electrocardiograms to alterative factors, particularly rotatory, gives promise of one type of clinical application.

5. Another form of clinical application may be the exploration in various pathologic conditions of "uncharted" areas in the Burger triangle.

REFERENCES

1. Brody, D. A., McKay, B. P., and Romans, W. E.: The Axostat: I. A New Instrument for the Multiaxial Registration of Extremity Electrocardiograms, AM. HEART J. **48**:589, 1954.
2. Graettinger, J. S., Packard, J. M., and Graybiel, A.: A New Method of Equating and Presenting Bipolar and Unipolar Leads of the Electrocardiogram, Am. J. Med. **11**:3, 1951.
3. Wilson, F. N., Johnston, F. D., and Kossman, C. E.: The Substitution of a Tetrahedron for the Einthoven Triangle, AM. HEART J. **33**:594, 1947.
4. Wilson, F. N., Johnston, F. D., Macleod, A. H., and Barker, P. S.: Electrocardiograms That Represent the Potential Variations of a Single Electrode, AM. HEART J. **9**:447, 1933.
5. Schmitt, O. H.: Cathode-Ray Presentation of Three-Dimensional Data, J. Appl. Physics **18**:819, 1947.
6. Schmitt, O. H., and Levine, R. B.: Direct Visual Examination of Stereovectorelectrocardiograms, Fed. Proc. **11**:140, 1952.
7. Milnor, W. R., Talbot, S. A., and Newman, E. V.: A Study of the Relationship Between Unipolar Leads and Spatial Vectorcardiograms, Using the Panoramic Vectorcardiograph, Circulation **7**:545, 1953.
8. Burch, G. E., Abildskov, J. A., and Cronvich, J. A.: Clinical Progress. Vectorcardiography, Circulation **8**:605, 1953.
9. Johnston, F. D., McFee, R., and Bryant, J. M.: An Integrating Circuit for Measurement of the Areas of Waves in the Electrocardiogram, Circulation **2**:5, 1950.

THE MEANING OF LEAD VECTORS AND THE BURGER TRIANGLE

DANIEL A. BRODY, M.D.

MEMPHIS, TENN.

THE relationship between the indirect leads of the electrocardiogram and the electromotive forces of the heart have been of interest since the earliest days of human electrocardiography. Waller[1] represented bipolar leads as the potential difference between two locations on the periphery of a variable electrical field generated by the heart. For purposes of simplification he treated the currents of cardiac origin as arising from a point source of electricity and flowing into a point sink. This concept has proved to be a useful one, and much of the electrocardiographic theory developed since Waller's time retains the idea that the electrical activity of the heart may be represented as one or more equivalent current dipoles.

Einthoven schematized the human body into a plane, electrically homogeneous volume conductor limited by an equilateral triangular boundary.[2,3] An equivalent cardiac dipole was located at the center of the triangular slab. The spacing between its poles was sufficiently close for the dipole to assume the characteristics of an electric doublet. Under these conditions Leads I, II, and III appeared to be the projections of an electrical vector upon the sides of the slab. This schema was attractive because it seemed to explain the observed fact that the deflection in Lead II was the sum of the deflections in Leads I and III (the Einthoven law). It is now recognized that this law is an inevitable algebraic relationship which is completely independent of the manner in which the electromotive forces of the heart produce potential differences between the extremities.[4] Nevertheless the Einthoven triangle has proved to be a valuable device in electrocardiographic interpretation as a frame of reference.

More recently Burger and van Milaan[5,6] have introduced the concept of the lead vector. They employed the lead vectors of the bipolar extremity leads to form a new type of triangle which presumably expresses the electrical relationships between the heart and the extremities more accurately than the Einthoven triangle. In general the Burger triangle is scalene (nonequilateral). Most expositions of the Burger concept have been in the language of vector mathematics. It is the primary purpose of this communication to restate the Burger

From the Cardiovascular Laboratory, Department of Medicine, University of Tennessee, Memphis, Tenn.

This work was supported by grants from the National Heart Institute, United States Public Health Service, and from the Memphis Heart Association.

Received for publication May 5, 1954.

concept in essentially nonmathematical terms. In addition, a method will be presented by which the Burger triangle may be transformed into a frame of reference comparable in usefulness to the Einthoven triangle and its associated triaxial and hexaxial reference systems.

THE LEAD VECTOR

The lead vector is a concise and accurate formulation of the physical characteristics of any electrocardiographic lead connection. Although the concept of the lead vector is somewhat abstruse, it is a physical entity in the same manner that other vectorial quantities such as force and acceleration are physically real.

In nonmathematical terms the significance of the lead vector may be appreciated from a descriptive analysis of the following situation: A volume conductor with a pair of electrodes applied to its surface contains a current dipole. No restrictions are implied regarding the size, shape, or electrical homogeneity of the volume conductor. The interpolar distance of the dipole is assumed to be relatively small. A point halfway between the poles of the dipole shall be referred to as its center. For purposes of convenience it shall be further assumed that the "strength" of the dipole (the product of its current times its interpolar distance) is unity. Given these conditions, what is the relationship between the dipole and the potential differences which it develops across the pair of electrodes?

With the center of the dipole fixed, its axis (line joining its poles) may be rotated until a unique position is found at which the potential difference produced across the pair of surface electrodes is maximal. This direction specifies the axis of the lead formed by the electrodes. For any other orientation of the dipole axis the potential difference developed across the pair of electrodes will follow the law of vector projection. That is, it will be the same as though a vector directed along the dipole axis, and having as its magnitude the maximum potential difference between the electrodes, were projected upon the lead axis.

For various positions of the pair of surface electrodes the direction of the lead axis will be different except in extremely fortuitous circumstances. Furthermore, the magnitude of the various maximal potential differences will be different. Thus it is seen that the electrical relationship of the electrode pair to the unit current dipole may be characterized by two measurable quantities: (1) the dipole *direction* at which the maximum potential difference occurs, (2) the *magnitude* of the maximum potential difference. Since vectors also are completely described by a magnitude and a direction, the physical characteristics of a lead connection may be referred to as its lead vector.

This concept, although relatively new, is not altogether foreign. The direction of a lead vector determines the axis of the lead. The length of the lead vector determines the "weight" of the lead. A familiar example of the weight of a lead is the relationship between the unipolar[7] (Wilson) and augmented unipolar[8] (Goldberger) extremity leads. The axes of the two types of leads are identical, but the weight of the Goldberger leads is 50 per cent greater than the corresponding Wilson leads. Therefore the contour of a given Goldberger lead is identical to the corresponding Wilson lead, but its amplitude is one-half again as great.[9,10]

The dipole itself also exhibits vectorial characteristics. The direction of the dipole vector is identical to its axis. The magnitude of the dipole vector is the product of its current strength times its interpolar distance. The lead itself is the dot (or scalar) product of the lead vector and dipole vector; i.e., lead = magnitude of the lead vector × magnitude of dipole vector × cosine of angle between the two vectors. The dimensions of the lead vector are volts /centimeter /ampere; the dimensions of the dipole vector are amperes × centimeters. The dimension of their scalar product, the lead, is in volts.

THE BURGER TRIANGLE

By applying the results of the preceding development, it is seen that a bipolar electrocardiographic lead may be treated as the scalar product of two parent vectors. One of these parent vectors is the equivalent cardiac dipole; the other is the lead vector. Since the Einthoven law is valid, it may be anticipated that the sum of the Lead I vector and the Lead III vector equals the Lead II vector. In terms of graphic representation this means that if the Lead I and Lead II vectors are plotted as arising from the same origin, and the Lead III vector is plotted as arising from the tip of the Lead I vector, the resulting configuration will be that of a closed triangle. That such a geometric relationship exists has been demonstrated by the Burger group,[5,6] ourselves,[9] and others.[11] It is this triangular configuration which Burger and van Milaan propose as "a new kind of triangle" to supplant the Einthoven triangle.

Since the Burger triangle is composed of lead vectors, it is clear that the orientation of the sides of the triangle represents the orientation of the axis of each of the conventional bipolar leads. Similarly, the lengths of the sides of the triangle indicate the weight of each bipolar lead.

The usefulness of the Burger triangle may be greatly enhanced by the type of development depicted in Fig. 1. A hypothetical Burger triangle composed of sides of relative length 4, 5, and 6 is shown in this figure. Each side is divided by a linear scale whose density of scale marks is proportional to the length of each side. Accordingly, the shortest side has 4 scale marks per unit length, the side of intermediate length has 5 scale marks per unit length, and the longest side has 6 scale marks per unit length. Constructing perpendicular lines to the sides of the triangle from each of the scale marks covers the figure with a triangular coordinate plot as shown.

In this manner the Burger triangle is transformed into a triangular coordinate system which represents a generalization of the Einthoven triangle in the following respects: (a) it obeys the Einthoven law; (b) it synthesizes a set of instantaneous scalar lead data into a unique, directed line segment within the triangle, or conversely (c) the representation of the electromotive forces of the heart as a single vector quantity may be projected on to the sides of the triangle to yield a set of scalar extremity leads.

The usefulness of the Burger triangle may be extended by plotting its medians (the lines joining each apex to the midpoint of the opposite side) in the form of another triangle. It was shown in a previous communication[9] that the medians

of the Burger triangle, when ascribed proper directional sense, are the lead vectors of the augmented unipolar extremity leads of the electrocardiogram. When this new triangle is provided with a coordinate network whose spacing is determined by the same principles outlined above in the case of the Burger triangle, it forms a new triaxial reference system applicable to the augmented unipolar

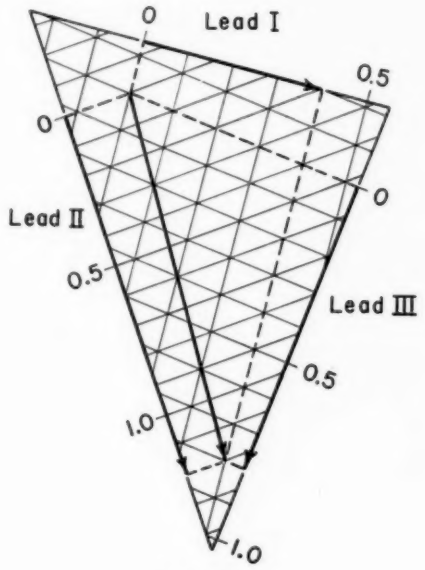


Fig. 1.

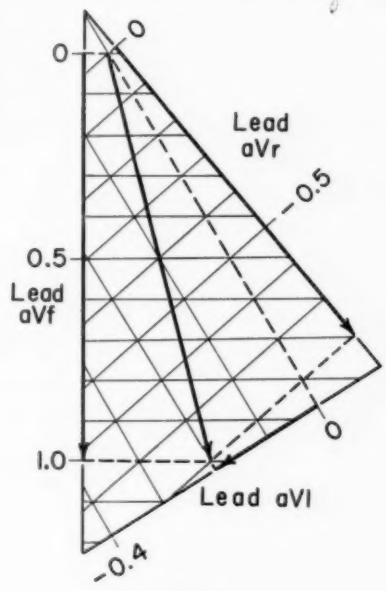


Fig. 2.

Fig. 1.—Illustration of the manner in which a Burger triangle may be transformed into a useful triangular coordinate plot. The projections of the heart vector on the sides of the triangle indicate the magnitudes of Leads I, II, and III. Because of the principles by which the spacing between scale marks is determined, the Einthoven relationship (I + III = II) is preserved. Note further that the projections of other line segments which join any two points within the coordinate plot obey the Einthoven law. Further description in the text.

Fig. 2.—Scalene triangle constructed from the medians of the preceding figure. The spacing of the triangular coordinate plot is determined by the same principles employed in Fig. 1. The projections of the heart vector on the sides of the triangle indicate the magnitudes of Leads aVr, aVl, and aVf. Note that this coordinate plot preserves the relationship aVr + aVl + aVf = 0.

extremity leads. It synthesizes unipolar lead data into a single, directed line segment within the triangle; conversely, if the electromotive forces of the heart are represented as a single vector within the triangle, the corresponding unipolar extremity leads may be determined by projecting the vector on the sides of the triangle. The scalar values thus determined obey the law that the sum of the three unipolar extremity leads at any instant is zero. This triangular coordinate system may be adapted for use with the Wilson extremity leads by increasing the spacing between the coordinate lines by 50 per cent.

When the so-called unipolar extremity leads are correctly recorded, simple and definite relationships exist among the extremity leads of the electrocardiogram. As examples, Lead aVf is one-half the sum of Leads II and III; Lead I is Lead Vr subtracted from Lead Vl; and the augmented unipolar extremity leads

are of the same configuration as the Wilson extremity leads except for a 50 per cent greater amplitude. When a set of such lead data is plotted in each of the two types of triangles described above, the directed line segments thus determined in the two systems are identical with regard to both length and direction. This suggests that the two reference systems can be combined into a single reference system. This may be accomplished by plotting the sides of the two triangles, and their scale markings, as arising from a single origin. For the sake of completeness the negative of each lead vector, together with the proper scale divisions, may also be plotted. Such a plot is shown in Fig. 3. The figure thus derived represents a generalization of the hexaxial reference system just as the Burger triangle represents a generalization of the Einthoven triangle.

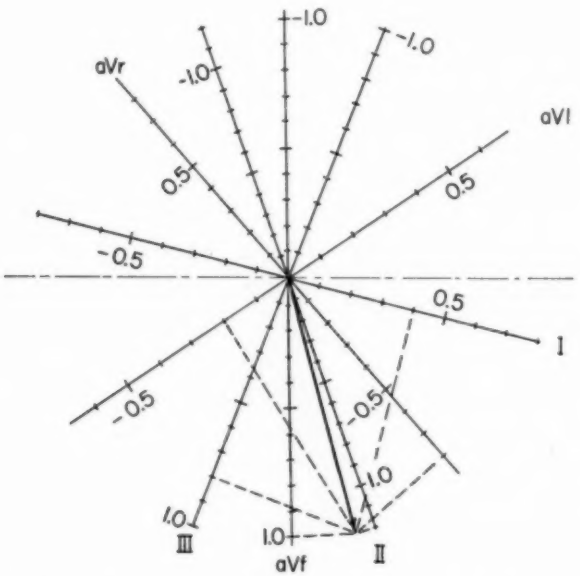


Fig. 3.—Hexaxial reference system constructed from the sides of the triangles shown in the two preceding figures. Note that all the algebraic laws of the extremity leads are preserved in this system: e.g., I + III = II, aVr + aVl + aVf = 0, aVl = ½ (I - III), I = ⅔ (aVl - aVr), etc.

DISCUSSION

In the limited case of electrical current flowing between a point source and sink in close apposition, there can be no serious doubt that lead vectors and the triangles (or other geometric configurations) formed from them accurately represent the physical characteristics of lead connections in volume conductors. The particularly remarkable aspect of the Burger concept is that it is applicable regardless of the size, configuration, and state of electrical inhomogeneity of the volume conductor. In these respects it represents a great theoretical advance over the simpler schematizations of the human body which have previously been proposed.

For a number of reasons, however, it is questionable that the Burger concept is strictly applicable to the human body. For one thing the heart occupies a

significantly large volume within the body, and therefore the electrical currents generated by the heart must be considered as arising from a great number of dipoles instead of a single dipole. Unfortunately, in our present state of knowledge there does not appear to be any theoretical basis upon which to formulate the concept of a "mean" lead vector which would apply with equal accuracy to all regions of the heart. Nevertheless, it is likely that a lead vector determined for a representative region of the heart (e.g., the center of its mass) would apply with reasonable accuracy to all portions of the heart. Furthermore, on the basis of experiments with models of the human body, it may be possible to form lead connections whose lead vectors are relatively invariant throughout the cardiac region.[12]

Other factors such as phasic variations in the configuration and electrical properties of the body must also be considered. The changes in the size and shape of the thorax during respiration are well known. Changes in the electrical impedance of the lungs during respiration are more obscure. Both of these factors may have an effect on lead vectors, and it is possible that respiratory changes seen in electrocardiograms are due in part to phasic changes in lead vectors as well as to variations in the position of the heart. It is also possible that the electrical impedance of the myocardium changes in a phasic manner during the heart beat, but the magnitude and direction of such changes are not well known at this time.

Despite these present uncertainties, the Burger triangle may eventually assume an important role in clinical electrocardiography. The preceding developments have indicated that any triangle can be transformed into a frame of reference which obeys Einthoven's law. The equilateral triangle is only one of an unlimited number of possibilities. It is not clear, however, at this time which triangular frame of reference is best suited for application to human electrocardiography. Several attempts have been made to determine Burger triangles for the human body,[13-15] but the methods employed in making such determinations cannot yet be accepted as being definitive. Nevertheless, it may be anticipated that a reasonably accurate Burger triangle will eventually be established for the human body. Possibly there will be a different triangle for each type of bodily habitus.

Regardless of the possibility of such future clinical developments, the concept of the lead vector is already proving useful at research levels because it admits the application of the powerful method of vector algebra to certain types of electrocardiographic calculations. A simple illustration of such an application is depicted in Fig. 4. The problem shown in this figure is, by assuming the conventional equilateral triangular frame of reference, to determine the lead connection which records the vertical component of the electromotive forces of the heart (Graettinger's lead vVf).[16] The problem is solved by drawing the Lead II and Lead III vectors as unit vectors arising from the same origin and directed at 60° and 120° respectively. The desired lead vector is shown as a unit vector arising from the same origin and directed vertically downward. Construction lines are drawn from the terminus of the vertical vector parallel to each of the

other two lead vectors, forming a parallelogram. The construction of this parallelogram represents the vertical lead vector as being the vector sum of portions of the Lead II and Lead III vectors. Because of symmetry of the figure, the portions of the vectors which constitute the components of the vertical lead vector are equal in magnitude. A simple trigonometric calculation shows that the magnitude of the portions involved is $1/\sqrt{3}$ of the unit vector length.

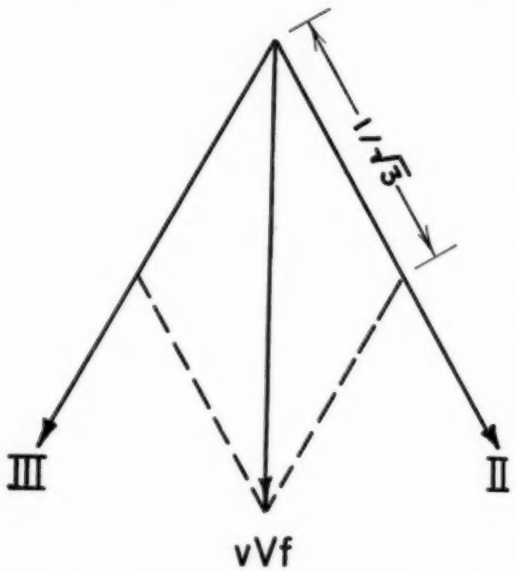


Fig. 4.—Illustration of the method by which vector mathematics may be employed to determine synthetic lead connections having certain desired properties. This figure deals with the calculation of a lead connection which will record the vertical component of the electromotive forces of the heart. Further description in the text.

Expressing this result in scalar notation,

$$vVf = (II + III)/\sqrt{3}.$$

Since, $Vf = (II + III)/3$ and $aVf = (II + III)/2$, we arrive at the result

$$vVf = \sqrt{3}\ Vf = 1.73\ Vf, \text{ or}$$

$$vVf = 2aVf/\sqrt{3} = 1.15\ aVf.$$

The above results show that in recording the vertical component of the cardiac vector the standardizing factor is 1.73 in the case of Lead Vf, and 1.15 in the case of Lead aVf. The same conclusions may be reached by relatively lengthy and tedious methods.[17] In contrast, application of the vector method achieves the solution with a few incisive mathematical operations.

In this laboratory the application of the lead vector theory has been extremely useful in the design of a new type of instrument which rotates the cardiac vectors with respect to the electrocardiograph.[18] As developments of this type continue, particularly if a scalene triangle is eventually adopted as an electrocardiographic frame of reference, vector methods should prove invaluable in determining standardizing factors and related types of information.

SUMMARY

1. The characteristics of an electrocardiographic lead connection may be represented by a physical entity known as the lead vector. The direction of the lead axis is the same as that of its vector. The relative "weight" of the lead is directly proportional to the length of the lead vector.

2. A closed geometric configuration, known as the Burger triangle, may be formed from the vectors of the conventional Einthoven leads. A method is presented for transforming the Burger triangle into a triangular coordinate system which obeys the Einthoven law. In general, the Burger triangle is not equilateral.

3. A similar coordinate system may be developed for the unipolar extremity leads. The two systems may be combined into a single hexaxial reference system which obeys all the algebraic laws of the extremity leads.

4. A scalene (nonequilateral) triangle, which represents the quantitative relationships between the electromotive forces of the heart and the extremity leads of the electrocardiogram with reasonable accuracy, may eventually supplant the equilateral triangle as a frame of reference.

5. The concept of the lead vector introduces the powerful method of vector mathematics into certain types of electrocardiographic calculations.

REFERENCES

1. Waller, A. D.: On the Electromotive Changes Connected With the Beat of the Mammalian Heart, and of the Human Heart in Particular, Phil. Tr. Royal Soc. London B **180**:169, 1889.
2. Einthoven, W., Fahr, G., and de Waart, A.: Ueber die Richtung und die Manifeste Grösse der Potentialschwankungen in Menschlichen Herzen und über die Einfluss der Herzlage auf die Form des Elektrokardiogramms, Arch. f. d. ges. Physiol. **150**:275, 1913.
3. Brody, D. A., Romans, W. E., and Little, R. C.: The Einthoven Triangle: An Observation Regarding the Validity of the Originally Proposed Triangular Representation of the Human Body, Science **116**:659, 1952.
4. Johnston, F. D., In Sodeman, W. A. (Ed.): Pathologic Physiology: Mechanisms of Disease, Philadelphia, 1950, W. B. Saunders Company, p. 92.
5. Burger, H. C., and van Milaan, J. B.: Heart-Vector and Leads, Brit. Heart J. **8**:157, 1946.
6. Burger, H. C., and van Milaan, J. B.: Part II, Brit. Heart J. **9**:154, 1947.
7. Wilson, F. N., Johnston, F. D., Macleod, A. G., and Barker, P. S.: Electrocardiograms That Represent the Potential Variations of a Single Electrode, Am. Heart J. **9**:447, 1933.
8. Goldberger, E.: A Simple, Indifferent, Electrocardiographic Electrode of Zero Potential and a Technique of Obtaining Augmented, Unipolar, Extremity Leads, Am. Heart J. **23**:483, 1942.
9. Brody, D. A., and Romans, W. E.: A Model Which Demonstrates the Quantitative Relationship Between the Electromotive Forces of the Heart and the Extremity Leads, Am. Heart J. **45**:253, 1953.
10. Langner, P. H., Jr., Benjamin, J. M., Jr., and Moore, S. R.: Certain Inevitable Relationships Among the "Unipolar" Extremity Leads, Circulation **5**:878, 1952.
11. Wilson, F. N., and Bayley, R. H.: The Electrical Field of an Eccentric Dipole in a Homogeneous Spherical Conducting Medium, Circulation **1**:84, 1950.
12. Brody, D. A., and Romans, W. E.: The Validity of Several Types of Vectorcardiographic Leads as Tested on a 2-Dimensional Model of the Human Body, J. Appl. Physiol. **6**:745, 1954.
13. Becking, A. G., Th., Burger, H. C., and van Milaan, J. B.: A Universal Vectorcardiograph, Brit. Heart J. **12**:339, 1950.
14. Den Boer, W.: The Clinical Value of Vectorcardiography, Acta Med. scandinav. **144**:217, 1952.
15. Wilson, F. M., Bryant, J. M., and Johnston, F. D.: On the Possibility of Constructing an Einthoven Triangle for a Given Subject, Am. Heart J. **37**:493, 1949.
16. Graettinger, J. S., Packard, J. M., and Graybiel, A.: A New Method of Equating and Presenting Bipolar and Unipolar Extremity Leads of the Electrocardiogram, Am. J. Med. **11**:3, 1951.
17. Cronvich, J. A., Conway, J. P., and Burch, G. E.: Standardizing Factors in Electrocardiography, Circulation **2**:11, 1950.
18. Brody, D. A., McKay, B. P., and Romans, W. E.: The Axostat: I. A New Instrument for the Multiaxial Registration of Extremity Electrocardiograms, Am. Heart J. **48**:589, 1954.

AN EQUIVALENT CIRCUIT FOR THE HUMAN HEART-BODY ELECTRICAL SYSTEM

ERNEST FRANK, PH.D.

PHILADELPHIA, PA.

INTRODUCTION

ELECTRICAL excitation of human heart muscle is accompanied by a complicated three-dimensional, time-varying current field within the body. Electric potentials produced by this current field can be measured conveniently at the body surface and reveal important information concerning the inaccessible heart generator. In measuring these body-surface voltages, various electric circuits are connected externally by means of electrodes in good contact with the skin. While the external electrical arrangements pose no basic problem of analysis, the complex internal electrical system of the body would appear to constitute a barrier preventing full exploitation of the powerful methods of circuit analysis. Yet the ability to analyze the entire system, taking into account internal as well as external effects in one composite network, is of considerable value in furthering an understanding of the limitations and performance of various electrocardiographic measuring arrangements.

EQUIVALENT CIRCUIT OF HUMAN ELECTRICAL SYSTEM

The application of circuit theory to any electrical system inevitably demands certain assumptions concerning the physical system.[1] Thus, in ordinary electric networks it is frequently assumed that the parameters of the system are constants (such as resistance, inductance, and capacitance), that the circuit elements may be "lumped" with no regard for their spatial extent or orientation, and that the effects of certain "stray" parameters may be ignored. The accuracy of the results of the analysis, therefore, depends upon the degree to which the assumptions are applicable to the actual electrical system under consideration. This type of limitation is likewise unavoidable in any equivalent circuit representation of the human electrical system. Consequently, it is important to recognize the basic assumptions which are made.

The equivalent circuit of the human electrical system to be evolved here has the virtue of being based upon a relatively small number of restrictive assumptions which are:

(1) The human body is a heterogeneous, linear, three-dimensional, irregularly shaped, resistive conducting medium.

From the Moore School of Electrical Engineering, University of Pennsylvania and the Edward B. Robinette Foundation, Medical Clinic, Hospital of the University of Pennsylvania, Philadelphia, Pa.

This work was supported in part by grants of the National Heart Institute, United States Public Health Service.

Received for publication May 7, 1954.

(2) The distribution of electrical forces associated with activation of heart muscle can be represented at each instant of time during the cardiac cycle by a single equivalent current dipole whose orientation and moment are variable.

(3) The equivalent current dipole remains fixed in position during the cardiac cycle.

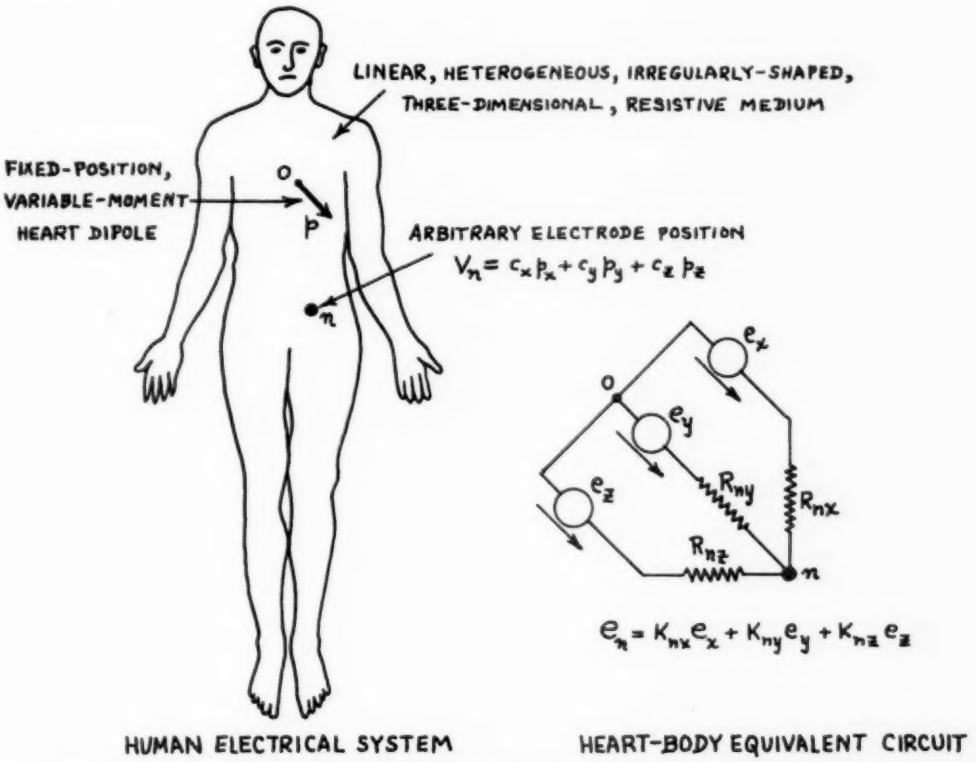


Fig. 1.—The assumptions regarding the human electrical system are portrayed on the left along with an equation describing the electric potential produced by the heart dipole of moment p at any arbitrary electrode location n on the body surface. On the right is shown an equivalent circuit which produces a potential at node n of the same form as at body position n. The shunting effect of the resistance from n to O has already been absorbed into the series resistors, and the voltages e_x, e_y, and e_z have been reduced accordingly. This shunt resistance largely determines the values of R_{nx}, R_{ny}, and R_{nz}, except for the contact resistance at the skin boundary, since it is only a few per cent of the actual resistance from the generator to O.

Future research in electrocardiography will furnish evidence concerning the degree to which these assumptions are applicable to the human subject. However, most existing practices in electrocardiography are based upon more stringent assumptions than those stated. For example, it is customarily assumed that the conducting medium is homogeneous, that the boundary of the human torso is spherical, that the equivalent current dipole is located at the center of the medium, and that body electrode positions (such as right arm, left arm and left leg) have particular locations with respect to the current dipole.[2] Such assumptions as these, most of which are gross approximations[3] introducing severe limitations, do not enter into the equivalent circuit to be developed here

which is applicable for any arrangement of linear inhomogeneities within the body, for any shape of the human torso, for any electrode positions, and for any fixed dipole position.

By adopting the three assumptions, it is possible to formulate a general relationship between the current dipole moment and the potential it produces at any point on the boundary of the medium.[4] The potential difference V between any point on the boundary and the mid-potential of the dipole, arbitrarily assigned the value zero, can be expressed as

$$V = c_x p_x + c_y p_y + c_z p_z \qquad (1)$$

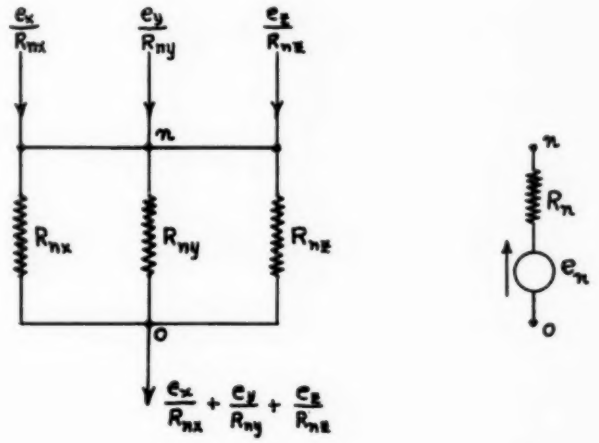
as a direct consequence of the linearity of the medium. The three rectangular components of the dipole are represented by p_x, p_y, and p_z which are functions of time, and the coefficients c_x, c_y, and c_z are real functions which depend upon the characteristics of the medium (size, shape, conductivity, and distribution of inhomogeneities), the position of the dipole, and the location of the point on the boundary where the potential is V. Equation (1) is essentially a statement of the law of superposition which is valid for any linear medium. It is a solution which satisfies Laplace's equation and boundary conditions in a three-dimensional medium of the kind postulated. The coefficients c_x, c_y, and c_z associated with a designated electrode position on the body surface are numerical constants for a given subject, since the medium characteristics are constant and the dipole position is assumed to be fixed.

The determination of an equivalent circuit for the human electrical system becomes one of developing an arrangement of generators and resistors which produce body-surface voltages in the general form of Eq. (1). Such a circuit, shown in Fig. 1, consists of three generators of voltage e_x, e_y, and e_z which vary with time in the same manner as p_x, p_y, and p_z, and three unequal resistors R_{nx}, R_{ny}, and R_{nz} connected from one terminal of each generator to the point n corresponding to any arbitrary electrode position on the human body. These resistors are dependent upon the characteristics of the medium, the location of electrode n, the fixed dipole position, and the contact resistance between the body electrode and the skin. Although it is difficult to determine accurately these resistor values for a human subject, rough approximations are usually sufficient for ordinary applications. The three generators are also connected to a common node 0 which corresponds to the dipole mid-potential. The voltage of node 0 is arbitrarily assigned the value zero, for convenience.

The body-electrode voltage at node n, symbolized by e_n, can be seen to have identical form to that of Eq. (1). The most expedient way to show this is to convert the voltage equivalent circuit of Fig. 1 to the node equivalent circuit[1] of Fig. 2, *A*. The potential difference $e_n - e_0 = e_n$ (with $e_0 = 0$) can then be written immediately from Fig. 2, *A* as the product of the total current $e_x/R_{nx} + e_y/R_{ny} + e_z/R_{nz}$ times the equivalent resistance of R_{nx}, R_{ny} and R_{nz} in parallel. Thus,

$$e_n = \frac{\dfrac{e_x}{R_{nx}} + \dfrac{e_y}{R_{ny}} + \dfrac{e_z}{R_{nz}}}{\dfrac{1}{R_{nx}} + \dfrac{1}{R_{ny}} + \dfrac{1}{R_{nz}}} = K_{nx}e_x + K_{ny}e_y + K_{nz}e_z \qquad (2)$$

which can be seen to be in exactly the same form as Eq. (1) where K_{nx}, K_{ny}, and K_{nz} correspond to c_x, c_y, and c_z. The equivalence of the circuit of Fig. 1 to the assumed human electrical system is thus established for the case of a single body-surface electrode of arbitrary location.



A. *B.*

Fig. 2.—The node equivalent circuit of Fig. 1 is shown at the left. The Thevenin equivalent is shown on the right where e_n is the open-circuit voltage at node *n* and R_n is the resistance of R_{nx}, R_{ny}, and R_{nz}, in parallel.

The circuits of Fig. 1 or 2, *A* may be simplified as shown in Fig. 2, *B* by the application of Thevenin's theorem.[1] The open-circuit voltage at electrode n is given immediately by Eq. (2) and the equivalent resistance, obtained by short-circuiting the electromotive forces, e_x, e_y, and e_z, can be obtained directly from Figs. 1 or 2, *A* as the parallel combination of the three resistors. Thus, so far as electrode n is concerned, it will behave electrically as though an internal voltage e_n given by Eq. (2) is acting in series with a resistance R_n, where

$$\frac{1}{R_n} = \frac{1}{R_{nx}} + \frac{1}{R_{ny}} + \frac{1}{R_{nz}} \quad . \tag{3}$$

This result may be extended to cases of two or more electrodes, as portrayed in Fig. 3, provided the internal resistance of the generators is neglected in comparison with the resistances from the generators to the boundary electrodes. Neglect of the generator internal resistance is justified because most of the current generated by the heart circulates within the medium in the near-vicinity of the heart. From a circuit point of view this corresponds to the existence of resistors completely inside the medium, connected directly across the heart generator terminals, which have values very small in comparison with the resistances from the generator terminals to the boundary electrodes. Consequently, regardless of the intrinsic internal resistance of the heart electromotive force, the effective output resistance of the heart generator will be negligible in comparison with the resistances to the boundary electrodes, since the heart generator is heavily shunted

internally by the conducting medium. Strictly speaking, the adoption of the dipole representation of the human heart implies a zero internal resistance heart generator, since the separation between the dipole source and sink is zero and the medium conductivity is finite.

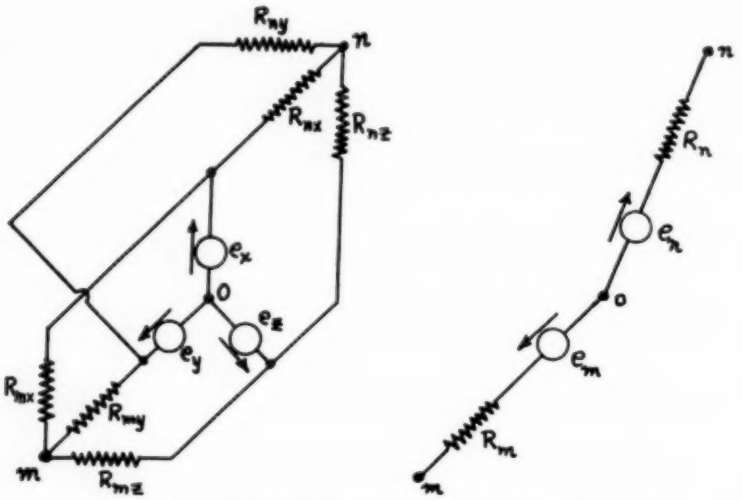


Fig. 3.—Application of the equivalent circuits of Figs. 1 and 2 to two electrodes m and n of arbitrary location is depicted on the left. The simplified equivalent circuit on the right is the most useful representation of the human heart-body electrical system.

APPLICATION

As an illustration of the way in which the equivalent circuit of Fig. 3 can be useful in furthering an understanding of the electrical effects to be expected from various circuit connections to the body, one important application which has not been analyzed in the literature will be given here; namely, the effects on measured heart signals of grounding the human subject. Grounding is a common practical problem, imposed by the existence of 60-cps. interference. Because of this interference, differential amplifiers must be employed in electrocardiographic practice, despite which the interference is frequently not eliminated. Grounding the subject often helps to reduce this interference. (The grounding is sometimes accomplished automatically by the input switching circuits of commercial electrocardiographic equipment.) However, the heart signal being measured can be altered by the ground connection to the subject, an eventuality that seems to have been ignored. The effects of grounding may be determined by direct experiment in those rare cases where little interference is encountered with the ungrounded subject. An experimental measure of the influence of grounding may always be obtained by introducing a low-impedance signal generator in the ground lead to determine the extent to which this signal interferes with the heart signal being measured. The equivalent circuit of Fig. 3 enables an analysis of the system, an estimate of the errors to be expected in the measured heart signals, and gives insight into the nature of the difficulties.

The situation to be analyzed is shown in Fig. 4 where a differential amplifier is shown connected to two electrodes, 1 and 2, of arbitrary location, the potential difference between which is the heart signal being measured. The switch S provides a ground connection from any other arbitrary point 3 on the body surface (the right leg ground connection, commonly used, is merely illustrative).

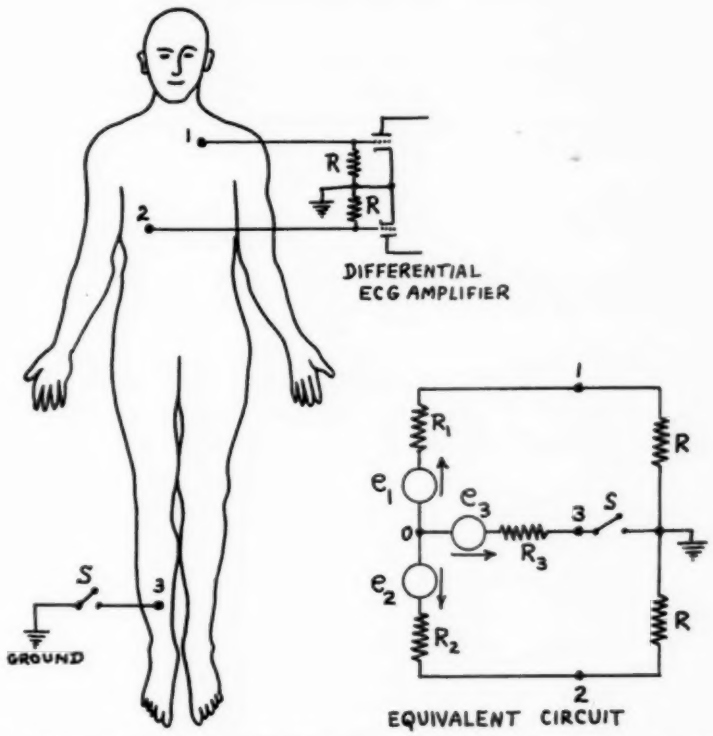


Fig. 4.—A differential amplifier is shown connected to two electrodes *1* and *2* of arbitrary location for the purpose of measuring the heart signal between them. Electrode *3*, also of arbitrary location, can be connected to ground via switch *S*. The equivalent circuit is given, based upon that of Fig. 3, and permits an analysis of the influence on the heart signal of grounding the subject.

Application of the equivalent circuit of Fig. 3 leads to the equivalent circuit of Fig. 4 in this case. It can be shown by straightforward circuit analysis that with S closed (grounded case) the potential difference between electrodes 1 and 2 is given by

$$V_1 - V_2 = \frac{e_1(R + R_2 + 2R_3) - e_2(R + R_1 + 2R_3) + e_3(R_1 - R_2)}{R + R_1 + R_2 + 2R_3 + \dfrac{R_1R_2 + R_1R_3 + R_2R_3}{R}}, \quad \text{S closed.} \qquad (4)$$

When the switch S is open (ungrounded case) this corresponds to allowing R_3 to go to infinity in Eq. (4) in which case it reduces to

$$V'_1 - V'_2 = \frac{e_1 - e_2}{1 + \dfrac{R_1 + R_2}{2R}}, \quad \text{S open.} \qquad (5)$$

If the differential amplifier input resistance is large compared with the internal body-plus-skin resistances R_1 and R_2, then $V'_1 - V'_2$ is approximately equal to $e_1 - e_2$, as expected. The difference between Eq. (4) and Eq. (5) gives the change in the signal voltage between electrodes 1 and 2 resulting from grounding the subject.

In the special case of $R_1 = R_2$, sometimes approached in practice, it can be shown that Eq. (4) reduces precisely to Eq. (5) regardless of the values of R_3 and e_3. This may be understood readily in terms of Fig. 4 where, if $R_1 = R_2$, the generator e_3 is applied to a balanced bridge and produces zero output across terminals 1 and 2; in other words, the "common mode" rejection (where e_3 is the common mode signal) is perfect for this case. Thus, there is no influence whatever on the heart signal being measured when the subject is grounded in the special case of $R_1 = R_2$.

However, if R_1 is not equal to R_2, which often occurs because of unequal rubbing of the skin beneath the electrodes or unequal conditions of electrode jelly, grounding the subject can alter the heart signal being measured. The change in heart signal is only a few per cent provided the internal resistances are smaller than one-tenth the amplifier resistance R. Indeed, the change in voltage owing to closing the ground switch S can be shown to be approximately $(R_1 - R_2)(e_1 + e_2)/2R$ if R is equal to or greater than ten times the internal resistances. Since this condition can be satisfied in practice, it is possible to state on the basis of this analysis that the influence of grounding the subject can be made slight as far as the heart signal is concerned.

Although grounding effects can be minimized by proper attention to circuit details, it does not necessarily follow that grounding errors are never present. For example, when central-terminal resistors are used which are large enough to make negligible the effects of skin resistance, it frequently turns out that the effective resistance seen from the amplifier input terminals is not small compared with the amplifier input resistance. In such cases the heart signal can be altered substantially owing to the ground connection.

CONCLUSION

It has been shown that an approximate equivalent circuit for the human subject can be established based upon the fixed dipole representation of the human heart assuming a linear, resistive medium. This equivalent circuit is useful in the analysis of a variety of electrocardiographic circuits such as investigating the influence of grounding the subject. Other applications include study of loading effects of external central-terminal resistors connected to the human subject,[5] prediction of errors in mirror-pattern circuits such as used by Schmitt and associates[6] and analysis of a wide variety of problems related to both research and practical aspects of electrocardiography. In some cases limited knowledge of the equivalent internal resistances necessitates semi-quantitative results, but there are numerous instances where a high degree of accuracy is possible with only an order-of-magnitude estimate of these resistances. Invariably, useful information can be obtained concerning soundness of methodology and sources of error due to

measuring equipment and techniques, often to a degree far more satisfactory than can be determined by direct experiment.

REFERENCES

1. Vail, C. R.: Circuits in Electrical Engineering, New York, 1950, Prentice-Hall, Inc.
2. Frank, E.: The Elements of Electrocardiographic Theory, A. I. E. E. Transactions (Communication and Electronics), May, 1953, p. 125.
3. Frank, E.: The Image Surface of a Homogeneous Torso, AM. HEART J. **47**:757, 1954.
4. Frank, E.: General Theory of Heart-Vector Projection, Circulation Research **2**:258, 1954.
5. Rappaport, M. B., and Williams, C.: An Analysis of the Relative Accuracies of the Wilson and Goldberger Methods for Registering Unipolar and Augmented Unipolar Electrocardiographic Leads, AM. HEART J. **37**:892, 1949.
6. Schmitt, O. H., Levine, R. B., Simonson, E., and Dahl, J.: Electrocardiographic Mirror Pattern Studies. Parts I, II and III, AM. HEART J. **45**:416, 500, 655, 1953.

FURTHER STUDIES ON OXIMETRY

PAUL SEKELJ, D. ENG.

MONTREAL, QUEBEC

WITH THE TECHNICAL ASSISTANCE OF CARL PINSKY, B.SC.,
CAROLINE CLEMENTS, B.SC., AND
MARYLEE PUTNAM, B.SC

IN a previous paper[1] we reported a new method and a new oximeter for the photoelectric determination of arterial oxygen saturation in man. The accuracy obtained with the instrument described when using a Millikan type of earpiece was found to be adequate for the clinical determination of the arterial oxygen saturation. Shortcomings resulting from the use of this earpiece were discussed. The purpose of the present communication is to report: (a) increased accuracy obtained when using a new type of earpiece with improved optical characteristics and one which is considerably smaller in size than the Millikan earpiece; (b) elimination of the hazard of earburn when using this type of earpiece; (c) increased accuracy and speed of readings when using a two-beam galvanometer built into the instrument; (d) a simple graphical calculating device which enables one to obtain the percent oxygen saturation quickly without the necessity of using slide rules or nomograms. Results obtained with several instruments suggest the possibility of constructing oximeters which could be calibrated with optical filters without significant variability in the expected accuracy. Continuous records of changes in arterial oxygen saturation and in "ear-thickness" obtained in normal subjects under varying respiratory activity, taken with a two-channel recording oximeter, will be presented. Possible sources of inaccuracy in the determination of arterial oxygen saturation when using the heat-flushed ear technique will be discussed.

INSTRUMENT AND EARPIECE

Figs. 1A and 1B are photographs of the oximeter and of the earpiece. Fig. 2 shows the cross-section view of the earpiece. The circuit diagram is shown in Fig. 3. It is noted that a built-in two-beam galvanometer is provided for simultaneous readings of the output currents of red and infrared filtered photocells. The operation and circuitry of the instrument are basically the same as previously described, with the exception that the present instrument is designed for both ear and whole blood oximetry. With the selector switch in positions 1 and 2 the instrument operates as a double-scale ear oximeter; in positions 3 and 4 as a double-scale whole blood oximeter; with the switch in position 5 either single-scale ear or whole blood operation is possible.

From the Department of Physiology, McGill University, and The Children's Memorial Hospital, Montreal, Quebec.

Aided by a grant from the National Research Council of Canada.
Received for publication May 21, 1954.

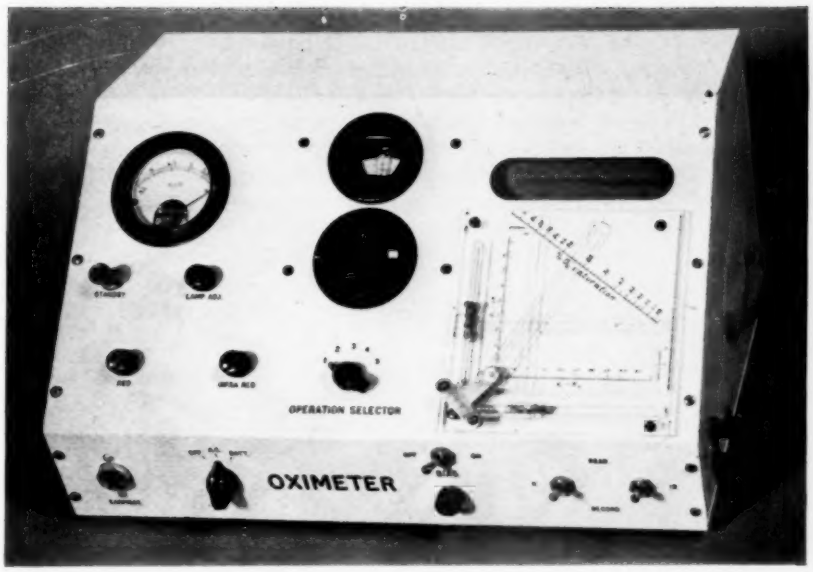


Fig. 1A.—Photograph of the oximeter.

Earpiece.—It has been generally considered that the dependence of the output of the infrared filtered photocell on the oxygen saturation of the arterial blood is one of the main sources of error in the accuracy of all types of existing oximeters. Elam and associates[2] have indicated that the infrared readings, using polychromatic light sources, are influenced considerably by variations in oxygen saturation. These workers found that certain selenium cells covered with Wratten filters No. 87 in three layers and No. 88 in two layers fulfill the requirements of independence of 0_2

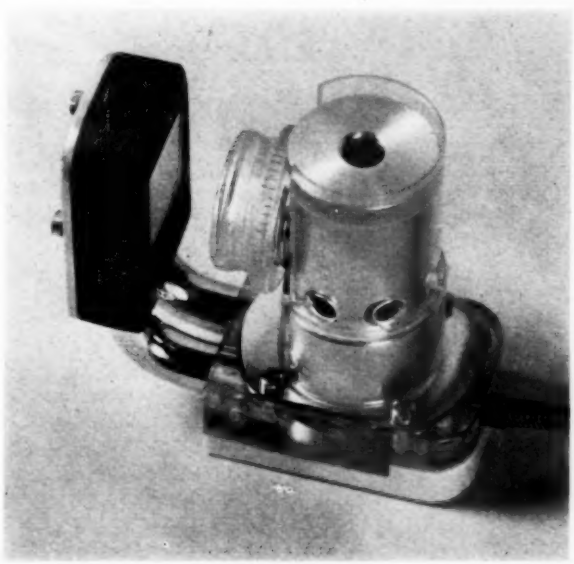


Fig. 1B.—Photograph of the earpiece.

saturation. During the calibration studies with the new earpiece, considerable attention was paid to the selection of photocell-filter combination to provide good sensitivity to changes in total hemoglobin without introducing unwanted effects due to changes in oxygen saturation. Of the various filters and combinations of filters studied by us with the ear oximeter, whole blood oximeter,* and the Beckman Spectrophotometer, the one made of two layers of Wratten 87 was selected. Wratten filter No. 29A has been used for the "red" photocell as previously described. Curves 1 to 5 in Fig. 4 show the relationship between the output of the photocell covered by two layers of Wratten 87 filters and the oxygen saturation over the full range from zero to 100 per cent.

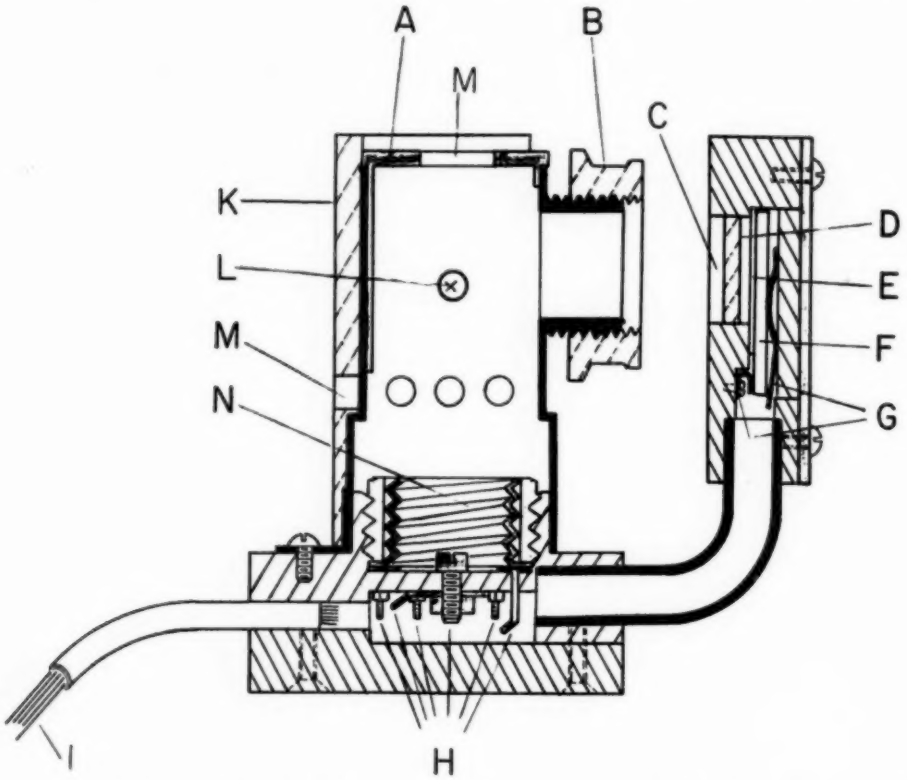


Fig. 2.—Cross-section view of the earpiece. *A*, Aluminum reflector. *B*, Lucite ring. *C*, Glass window. *D*, Lucite window. *E*, Gelatin filters. *F*, Photocells. *G*, Photocell contacts, front and back. *H*, Terminals for cable. *I*, Cable, 5 wire. *K*, Lucite sleeve. *L*, Lamp. *M*, Holes for heat radiation. *N*, Lamp socket assembly.

These were obtained on samples drawn from five subjects during cardiac catheterization by using the whole blood oximeter with the blood stationary in the cuvette. Points of 100 per cent oxygen saturation were obtained by bubbling pure O_2 for 10 minutes through the blood sample in a container in which was placed minute quantities of silicon jelly (Dow Corning Antifoam A) to prevent foaming. Points at zero per cent saturation were obtained by reduction with $Na_2S_2O_4$. A slight scatter at points of 100 per cent saturation is likely due to some hemolysis occurring during oxygenation. Measurements on a dog's arterial blood in both red (R) and infrared (IR) bands are shown in records 5A and 5B. In record 5A the output of both photocells with the dog's heparinized arterial blood flowing in the cuvette is shown. Record 5B represents measurements on the same

*A paper describing the whole blood oximeter which has been developed as a joint project of The Children's Memorial Hospital and the Department of Physiology, McGill University, will be shortly submitted for publication.

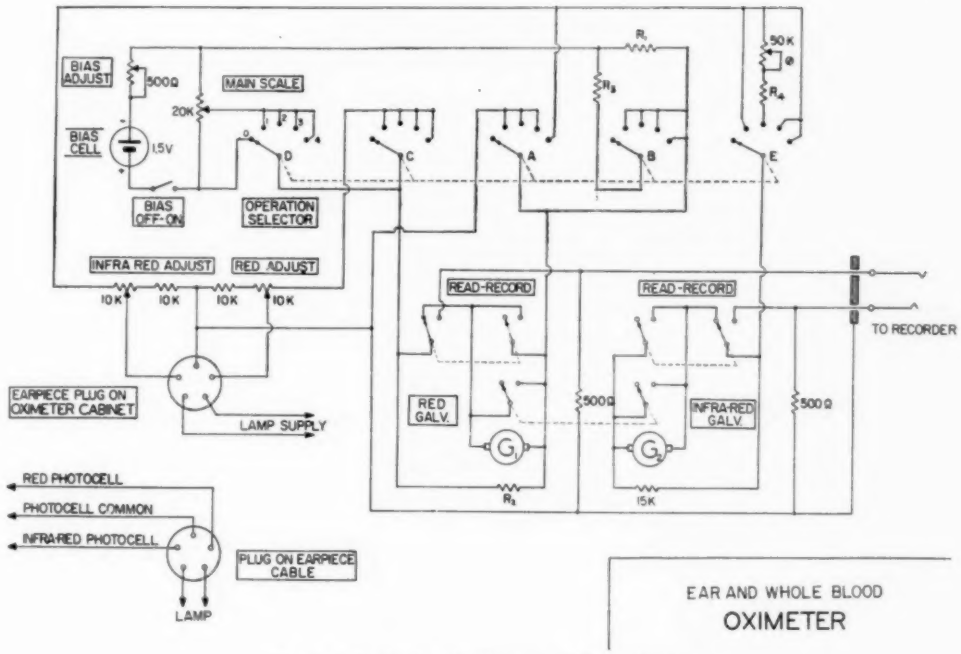


Fig. 3.—Basic circuit diagram of the oximeter.

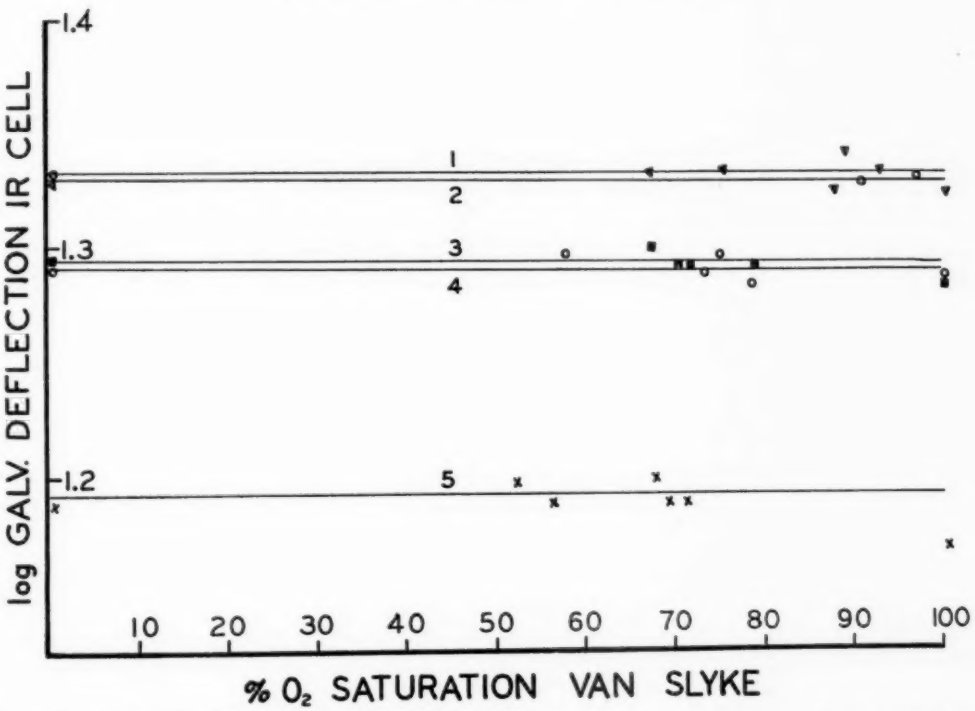


Fig. 4.—Relationship between the output of the photocell covered by two layers of Wratten 87 filters and the oxygen saturation. Measurements carried out on whole blood samples with the cuvette oximeter with the blood stationary in the cuvette.

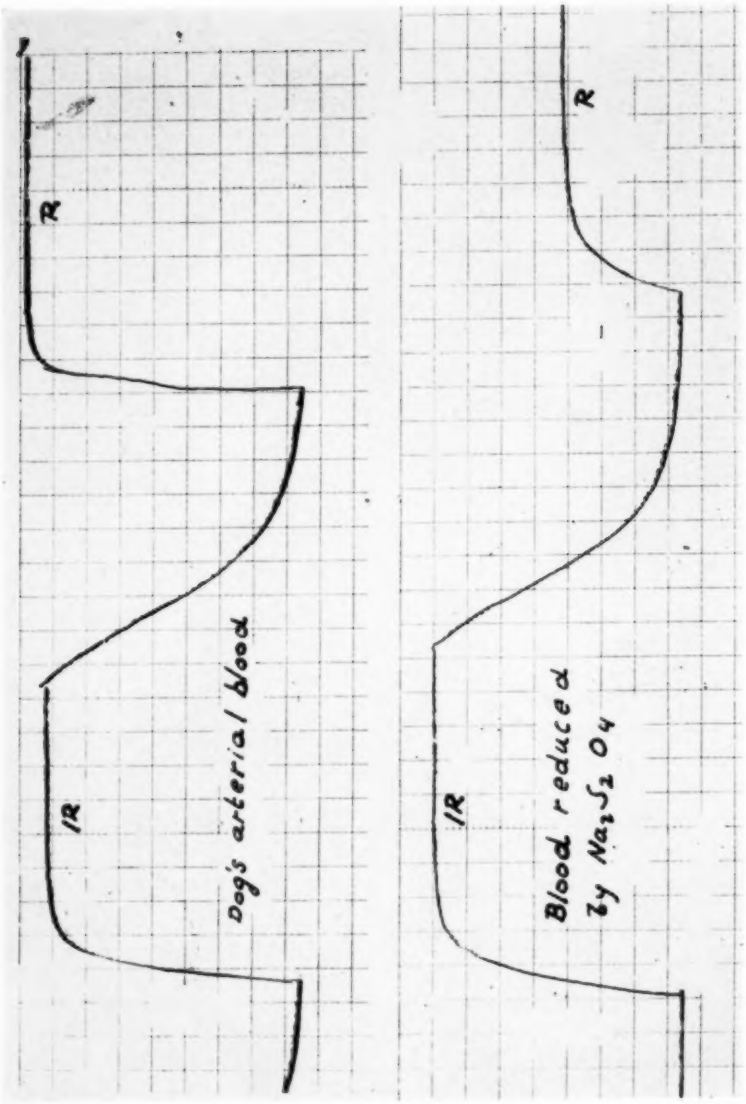


Fig. 5.—*A* and *B*. Measurements on a dog's arterial samples in both red and infrared bands with the cuvette oximeter.

blood after total reduction by $Na_2S_2O_4$. Close inspection of these records shows that there is practically a negligible difference of the order of 2 per cent in the IR reading at these two levels of oxygen saturation. It is noted that the sensitivity of the recording system was adjusted so that 100 μV resulted in a 5 cm. deflection on the recorder. The controls of both R and IR photocells were adjusted to cause nearly equal deflections with the dog's arterial sample in the cuvette. The independence of the output of the infrared filtered photocell from the degree of oxygen saturation is further illustrated by the record shown in Fig. 6. In this experiment two fractions of a human blood sample, one oxygenated, the other reduced by evacuation with a water pump, were continuously mixed while flowing through the cuvette. The outputs of both photocells were recorded simultaneously. The deflection sensitivity of the recording system in this experiment was 25 μV/cm. for the red and 5 μV/cm. for the infrared channel. In spite of this very high degree of sensitivity there is no visible change in the output of the IR filtered photocell at different levels of oxygen saturation.

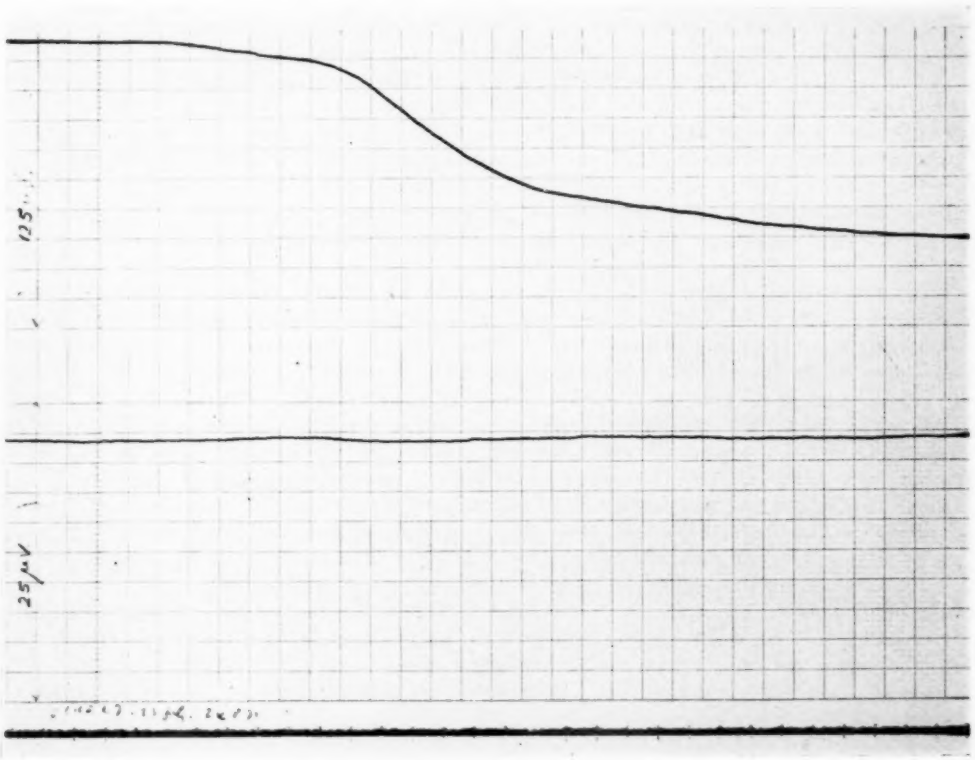


Fig. 6.—Record of the transmission with both red and infrared filtered photocells when two samples of human blood, one oxygenated, the other reduced, are continuously mixed while flowing through the cuvette.

Calibration of Oximeters by Use of Optical Filters.—One of the major practical difficulties encountered in oximetry is the fact that because of different spectral characteristics of individual photocells it is necessary to calibrate each earpiece by comparison with gasometric determinations on simultaneously drawn arterial samples. This is a laborious and delicate procedure. Furthermore, the useful lifetime of an earpiece is rather limited due to fatigue and to changes in the spectral characteristics of the photocells. In order to make the calibration of individual oximeters less burdensome, attempts have been made to perform the calibration by comparison with optical filters.

Photocells were carefully selected for similar spectral response. The first step in the procedure of calibration consisted in adjusting the electrical circuits of the individual instruments to produce nearly equal deflection ratios of the red and infrared filtered photocell currents with the optical filters in the earpieces. It may be of interest to note that galvanometers of three different makes but of similar order of sensitivities were used. The optical filters were constructed to simulate the transmission of both red and infrared light through ears of varying "thicknesses" in normal subjects breathing room air.

It was intended to establish the values of constants a, m, and f in the expression

$$D_r = f.m.\ \log C(D_i - a),\ (Eq.\ 9,\ p.\ 835).^1$$

In the present case, a represents the intercept on the abscissa, m the slope of the line, and f the galvanometer deflection in millimeters per scale division.* D_r and D_i are the red and infrared filtered photocell currents at the beginning of the experiment while the subject is breathing room air or pure O_2 and C is the hemoglobin concentration in grams per 100 ml. It had been hoped that once these constants were established, the percentage oxygen saturation values for all the instruments adjusted with optical filters could be read off the same calibration diagram. To test the validity of this assumption and check the accuracy of the determinations of the arterial oxygen saturation, two series of experiments were carried out. The object of the first series was to establish a single calibration diagram for four individual instruments and to determine the accuracy of each instrument separately and of the group, by taking the line of best fit as line of calibration. In the second set of experiments the calibration diagram thus obtained was used in carrying out determinations of the absolute values of oxygen saturation with a fifth instrument in subjects with cardiovascular anomalies and/or suspected hypoxia.

In the first set of experiments forty-one radial artery blood samples at different levels of O_2 saturation were withdrawn from nine normal healthy subjects. Procedure and calibration were the same as described previously. The single calibration diagram for four units (instruments and earpieces) constructed from oximeter readings and from values determined by the Van Slyke method of analysis on simultaneously drawn arterial samples is shown in Fig. 7. The standard deviations of differences between the values obtained from gasometric determinations and the line of best fit, in per cent oxygen saturation, for the individual instruments were: 1.096; 2.437; 2.110; 2.375; and for the group was 2.0047. It should be noted in relation to this observed accuracy that these determinations were made under favorable conditions, i.e., in healthy subjects of approximately the same age group. Thirty-four out of forty-one determinations at levels between 62 and 100 per cent arterial oxygen saturation showed a difference between the photoelectrically determined values and those obtained by the Van Slyke method within less than ± 2 per cent, four were within ± 4 per cent, two were within ± 5 per cent, and one showed a difference of 5.2 per cent.

Results obtained in the second series of experiments are shown in Table I†. In this table values of the per cent O_2 saturation determined with the fifth oximeter are compared with those obtained by the Van Slyke method in thirty-two subjects with cardiovascular anomalies. The subjects, whose age varied between a few weeks and 38 years, were breathing room air while readings were taken. Age, sex, hemoglobin concentration, condition of patients during the sampling period, and diagnosis are tabulated.

The standard deviation of differences in per cent O_2 saturation, in the range from 48 to 100 per cent, was 2.9. It should be pointed out that with the exception of two adults the subjects

*It will be recalled that the circuit arrangement comprises a bias cell, and the scale serves as a very accurate means to measure the bias current which flows in the circuit. This circuit arrangement represents basically a "null-bridge" method. Thus when the bridge is balanced by rotation of the scale, the reading is a measure of the output of the red filtered photocell. The readings of the infrared cell current are directly taken on the lower scale of the two-beam galvanometer incorporated into the instrument. Considerable simplification in the operation results by introducing into the expression the values of D_r in scale divisions and those of D_i in millimeters galvanometer deflection, making thus f = 1.0.

†This table has been prepared by Miss Caroline Clements and Miss Marylee Putnam, who carried out the oximetric and gasometric determinations during the past year at The Children's Memorial Hospital, Montreal. With reference to the data presented in the above table it should be noted that in two cases the results were discarded. In the first instance, the earpiece could not be properly fitted because of abnormal anatomy of both ears of the subject. In the second case, the result was rejected because of incorrect operation of the instrument due to damage to a galvanometer suspension.

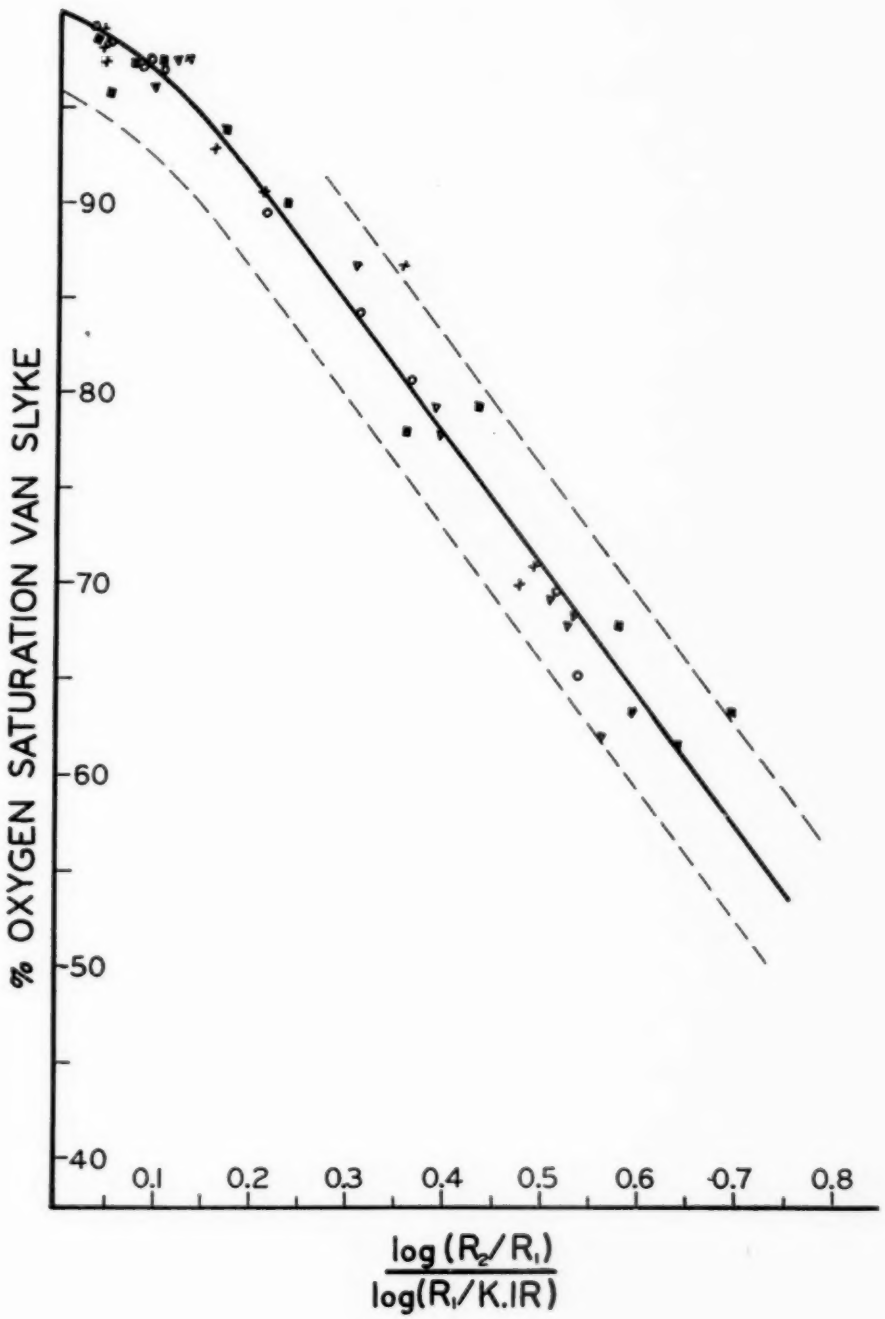


Fig. 7.—Calibration diagram for four individual oximeters preset with optical filters constructed from oximeter readings and from values determined by the Van Slyke method of analysis on simultaneously drawn arterial samples.

TABLE I

NO.	SUBJECT	DATE (1953)	AGE	SEX	HEMOGLOBIN (GRAM/100 ML.)	% O_2 SATURATION		CONDITION OF PATIENT	DIAGNOSIS
						VAN SLYKE	OXIM.		
1.	M.B.	1/26	2½ yr.	F	10.85	92.5	93	Crying	Eisenmenger complex (?)
2.	R.K.	1/30	38 yr.	M	21.7	86.1	84	Quiet	Suggestive of Eisenmenger complex with marked pulmonary hypertensive changes
3.	I.G.	2/4	4 yr.	M	11.8	94.6	94	Quiet	Patent ductus arteriosus
4.	R.H.	2/13	4 yr.	M	12.0	94.4	95.7	Quiet	Two pulmonary veins, R.A.; flow of blood from R.A. to L.A.
5.	C.S.	2/23	14 yr.	M	13.7	99	96.2	Quiet	Septal defect, probably auricular
6.	J.H.	2/27	27 yr.	M	15.9	89	86	Quiet	Possible Eisenmenger complex with pulmonary hypertension
7.	E.S.	3/16	11 yr.	F	12.0	97.9	97.3		Atrial septal defect or anomalous drainage, pulmonary veins
8.	E.O.	3/26	10 yr.	F	15.7	68.7	74.1	Quiet	Pulmonary hypertension
9.	D.G.	3/31	11 yr.	F	14.8	95	91	Quiet	Pulmonary stenosis with L. to R. shunt through ventricular septal defect
10.	J.L.	4/16	32 yr.	M	12.5	72.5	77.8	Quiet	Pulmonary hypertension, primary or secondary to changes occurring in lung parenchyma
11.	C.H.	5/14	5 yr.	F	11.65	99.0	96.4	Crying	Pulmonary hypertension, ventricular septal defect or patent ductus and pulmonary regurgitation
12.	F.F.	5/15	10 yr.	F	17.0	84.8	88.0	Screaming and quiet	Tetralogy of Fallot
13.	R.F.	5/21	5 yr.	M	11.61	90.6	87.5	Alternately quiet and crying	Tetralogy of Fallot, postoperative
14.	H.S.	5/28	6 yr.	F	11.6	95.6	99.0	Quiet	Isolated infundibular stenosis
15.	R.R.	6/4	11 yr.	M	12.5	96.0	98.0	Crying	Pulmonary valvular stenosis
16.	E.M.	6/8	3 yr.	M	18.9	67.7	64.2	Crying	Tetralogy of Fallot, postoperative
17.	R.F.	6/18	3 yr.	M	19.4	49.2	52.0	Quiet	Tetralogy of Fallot
18.	C.B.	6/19	9 mo.	F	14.25	62.4	66.5	Crying	Pulmonary hypertension, undiagnosed
19.	R.C.	6/25	7 yr.	M	13.7	95.6	96.5		Pulmonary stenosis, infundibular type
20.	R.R.	7/3	11 yr.	M	12.8	96.0	95.0	Screaming	Pulmonary valvular stenosis, postoperative
21.	R.F.	7/7	3 yr.	M	16.5	72.0	74.0	Crying	Tetralogy of Fallot, postoperative
22.	J.M.	7/9	4 yr.	F	11.1	93.0	97.0	Crying	Interatrial septal defect or anomalous pulmonary venous return
23.	N.B.	7/13	4 wk.	F	16.5	92.1	92.5	Crying	Undiagnosed
24.	M.K.	7/16	11 yr.	F	13.3	97.0	94.0	Crying slightly	Anomalous drainage pulmonary veins, superior vena cava

(Continued on oppsoite page.)

TABLE I (CONT'D)

NO.	SUBJECT	DATE (1953)	AGE	SEX	HEMOGLOBIN (GRAM/100 ML.)	% O_2 SATURATION		CONDITION OF PATIENT	DIAGNOSIS
						VAN SLYKE	OXIM.		
25.	R.R.	8/4	4 yr.	M	9.9	96.0	95.5	Crying	Ventricular septal defect
26.	D.B.	8/6	7 yr.	F	14.7	97.0	97.0	Crying	Reverse patent ductus
27.	R.P.	9/10	3 yr.	M	19.5	49.5	48.5	Sleeping	Tricuspid atresia
28.	N.D.	9/25	3 yr.	F	10.0	95.0	96.0	Quiet	Auricular septal defect
29.	B.W.	10/9	6 yr.	M	13.7	94.0	96.0	Quiet	Postoperative Tetralogy of Fallot
30.	C.R.	10/9	9 mo.	F	16.7	66.0	74.0		Undiagnosed
31.	R.B.	11/9	3 yr.	M	12.7	90.5	90.0	Crying and quiet	Postoperative Tetralogy of Fallot
32.	S.S.	11/26	2½ yr.	F	11.1	96.5	96.0	Crying	Interventricular septal defect

were children and infants. In many instances accurate visual recording of the oximeter reading is impossible because even the slight body movements or crying of the children may cause rapid excursions of the galvanometer spot. Thus readings obtained from average visual observations and those from blood samples withdrawn at certain rates cannot be considered truly simultaneous. It appears to be very difficult, if not impossible, to differentiate between the error caused by this factor and the random errors inherent in the method of testing. In some cases uncertainty exists as regards the arterial sample itself. It is supposed that a similar situation exists in subject No. 30, Table I. As no further arterial puncture was performed in this subject, the question remains unsettled whether the aliquot was arterial, a mixture of arterial and venous, or venous blood. Disregard of this experiment would change the standard deviation of differences from 2.9 to 2.65.

In spite of these uncertainties in evaluation of existing errors in simultaneous determinations of the arterial O_2 saturation by both methods, it appears that the results obtained with oximeters preset with optical filters are satisfactory. The mean value obtained for the standard deviation of differences of the determinations in adults and in children was 2.56.

Calculator for Use With the Oximeter.—Apart from the laborious calibration procedure and the variation between different earpieces, one of the disadvantages of the method previously described is that the computation of the value of the oxygen saturation had to be performed by using slide rules or logarithmic tables and reference had to be made to empirical calibration diagrams. The nomogram previously described facilitated somewhat the computation, but in order to avoid this inconvenience a calculating device has been designed and incorporated into the instrument. With the use of this device, a drawing of which is shown in Fig. 8, the use of the oximeter is greatly simplified. The operation of this calculator is extremely simple and readings of the galvanometer and dial scale can be converted in per cent oxygen saturation in a matter of seconds, without significant decrease in the accuracy. It performs the computation of the ratio,

$$\frac{\log D_{rx} - \log D_{ri}}{\log D_{ri} - \log (K \cdot D_i)}, \text{ (Eq. 7a, p. 843).}^1$$

The position of the vertical scale cursor corresponds to the value of the denominator and the position of the horizontal-scale cursor to that of the numerator in this expression. In order to simplify the writing, R–IR is used here to denote $\log D_{ri} - \log (K \cdot D_i)$ and R_1–R_2 to denote $\log D_{rx} - \log D_{ri}$. When using the calculator the readings are taken on logarithmic scales. Both instrument dial and galvanometer scales are provided with a linear upper and a logarithmic lower scale. The operation of the oximeter is by a "null" method, i.e., as the arterial O_2 saturation decreases and the galvanometer spot moves to the right, it is restored to the zero position by rotation of the instrument dial. All results reported in Table I were obtained by using the calculator.

An electronic computing oximeter, in an advanced stage of development in this laboratory, makes use of the principle on which this calculator is based to perform the computations.

DIRECT-WRITING OXIMETER

Optical, electrical, and electronic techniques to provide continuous direct-writing records of arterial oxygen saturation in man have been reported.[3-5] It is outside the scope of this paper to review the differences between the recording techniques of others and those used by the present authors. The principles upon which the recording system is based will be briefly described and some aspects pertaining to the general field of oximetry examined.

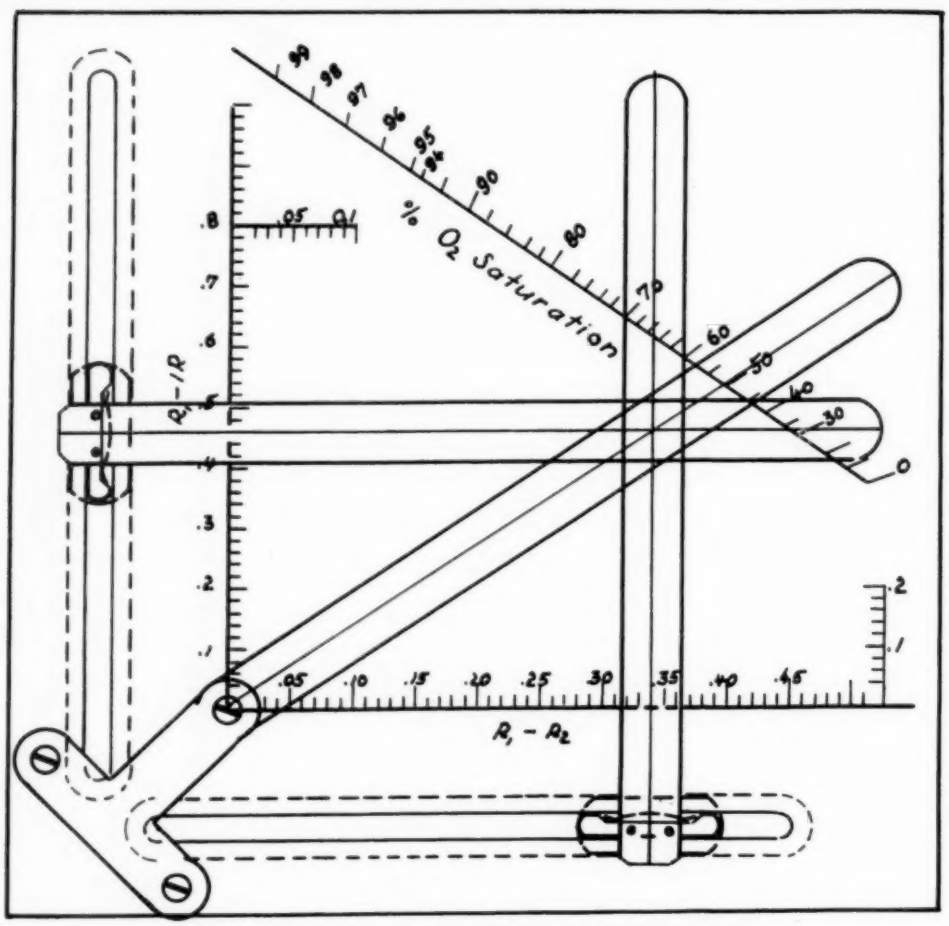


Fig. 8.—Photograph of a drawing of the calculating device.

The Recording System.—The earpiece described here was used in these studies and two specially designed chopper-type amplifiers were employed. The carrier frequency of the chopper was 60 cycles per second. The time constants of the amplifying systems were adjusted to allow the stylus of the recorder to reach 90 per cent of the maximal deflection in one second or less. This may be considered as a sufficiently fast response to make the instrumental lag negligible

and to record faithfully changes in blood volume and oxygen saturation. By means of simple switching, readings could be taken either with the oximeter galvanometer or with the pen recorders (Sanborn Twin-Viso Recorder). In this manner the stability of the photocell output, the linearity, and zero-line stability of the amplifying system could be easily checked. A definite preset relationship between the sensitivities of the galvanometer and of the recording system has made it possible to quickly convert the information obtained from the R and IR records into per cent oxygen saturation by using the calculating device shown in Fig. 8. This is possible only under the condition that the load into which the photocells work is comparable in magnitude for both the internal resistance of the galvanometer and the input resistance of the recording oximeter. The choice of an effective D.C. input resistance of about 250 ohms for the amplifiers seems to fulfill this condition. The value of this input resistance is unusually high for the type of amplifiers used, and the selected speed of response presented a number of difficulties of design and shielding. The recording sensitivity mostly used was 10 μV/cm. for the red and 5 μV/cm. for the infrared channel, respectively.

"Arterialization" of the Capillary Blood in the Pinna by Radiant Heat.—Most investigators agree that the heat provided by the light source of the earpiece does not result in blood saturated with oxygen as in arterial blood, but the main point of contention is the degree of this difference, and whether it is a major source of inaccuracy and variability in oximetric determinations. An attempt has been made to investigate this point by means of simultaneous continuous recording of the changes in the red and infrared transmission bands in healthy human subjects.

The Valsalva experiment, by interfering with the venous return, results in an increased blood volume and pressure in the vessels of the pinna, and therefore this maneuver was carried out on normal human subjects in order to show the effect of a sudden change in the blood volume on the oximeter readings. It will be recalled that changes in the blood volume influence the outputs of both photocells, while changes in the oxygen saturation influence only that of the red-filtered photocell. It is restated that the relationship existing between the deflections with the red, D_r, and Infrared, D_i, photocells is defined by:

$$D_r = m \log C (D_i - a).$$

Ten minutes after placing the earpiece on the pinna the subjects performed the Valsalva experiments following inhalation of pure oxygen for five minutes and repeated this maneuver after having breathed room air for six minutes. Results obtained in ten healthy subjects of both sexes are shown in Table II. In this table the recorded values of D_r, D_i, and the calculated values of the deflection ratio $n = m \log C = \frac{D_r}{D_i - a}$ are tabulated. In order to eliminate the individual factor, log C, the ratio $p = \frac{n'}{n}$ was established, the values of which are contained in the last two columns of this table. The values marked by the prime, ′, refer to measurements taken during the experiments when the light transmission with both red and infrared filtered photocells were minimum, indicating a maximum blood volume in the light path.

TABLE II

SUBJECT	POSITION	BREATHING OXYGEN						BREATHING AIR						p	
		BEFORE EXPER.			DURING EXPER.			BEFORE EXPER.			DURING EXPER.				
		D_r*	D_i†	n	D_r'	D_i'	n′	D_r	D_i	n	D_r'	D_i'	n′	OXYGEN	AIR
P.S.	Sitting	30.50	20.00	1.9062	27.00	17.50	2.0000	28.50	20.00	1.7812	25.30	17.60	1.8603	1.0492	1.0444
D.St.	Supine	34.50	21.50	1.9714	31.80	19.23	2.0880	33.00	21.50	1.8857	28.95	18.50	1.9965	1.0591	1.0587
D.C.	Sitting	35.60	22.00	1.9778	30.76	18.80	2.0784	34.20	22.00	1.9000	28.60	18.27	2.0042	1.0508	1.0548
A.R.	Sitting	31.20	19.80	1.9750	29.00	18.13	2.0524	30.80	20.00	1.9250	28.04	17.87	2.0216	1.0392	1.0518
G.M.	Supine	32.40	20.20	2.0000	30.50	18.80	2.0608	30.20	19.60	1.9359	27.28	17.80	1.9768	1.0400	1.0211
L.P.	Sitting	26.80	16.90	2.0775	24.80	15.44	2.1678	25.20	16.50	2.0160	22.70	14.97	2.0693	1.0435	1.0264
P.R.	Sitting	30.40	19.20	2.0000	27.20	16.87	2.1134	28.70	18.80	1.9392	24.30	15.87	2.0472	1.0567	1.0557
C.F.	Supine	22.10	17.60	1.6250	19.30	15.34	1.7019	20.00	16.80	1.5625	17.06	14.22	1.6693	1.0473	1.0683
J.P.	Sitting	39.00	24.50	1.9024	36.44	22.63	1.9559	37.50	24.30	1.8473	35.12	22.63	1.8851	1.0281	1.0205
C.F.	Supine	32.00	16.70	2.5197	28.84	14.835	2.6617	30.30	16.70	2.3858	26.06	14.30	2.5300	1.0563	1.0604
													Mean:	1.0511	1.0525

*The D_r values are expressed in scale divisions, 1 scale division = 4.55 mm. galvanometer deflection.
†The D_i values are expressed in mm. galvanometer deflections.

The results obtained, in particular the nearly identical values for p in all subjects either on oxygen or room air, make it apparent that the oximeter measures blood of the same or very nearly the same oxygen content at the beginning and during the Valsalva maneuver. This in turn would indicate that the heat provided by the light source of the earpiece results in adequate arterialization of the blood at the site of the measurements in these subjects. Changes in the value of the constant p might be expected if the oxygen saturation of the blood in the area directly heated by the light beam were to differ significantly from that in the capillaries of the inadequately heated surrounding tissues. In order to illustrate the effect of small changes in oxygen saturation on the p-value it was calculated that in Subject D.C., if the oxygen saturation had been 2 per cent lower when the ear blood volume was maximum during inhalation of oxygen, the p-value would have changed from 1.0508 to 0.998. Under similar conditions the p-value would have decreased from 1.0281 to 0.985 in Subject J.P. The magnitude of these changes in the p-value of the order of 4 to 5 per cent appears to be significant in view of the accuracy of these determinations in establishing the mean value of p to be equal to 1.0511 (1.0281-1.0591) and 1.0525 (1.0205-1.0683) for oxygen and room air, respectively. The variability in the p-values obtained in the experiments on room air appears to be somewhat greater than that with those following inhalation of oxygen. It cannot be demonstrated with certainty whether this variability is due to the occurrence of slight changes in the oxygen saturation during the experiments or is due to experimental errors.

Another indirect way to examine to what extent the blood contained in the capillaries in the path of the lightbeam is "arterialized" is to compare the values of the deflection ratio, n, obtained in different subjects when breathing varying gas mixtures. We felt that the choice of pure O_2, air, and 12 per cent O_2 for breathing mixtures could serve as a reasonable basis to carry out these comparisons. If the blood at the site of the measurements were not essentially arterial and/or if a significant amount of venous admixtures were present, then one might expect to find a comparatively large difference in the n-values obtained for pure O_2 and air as compared with that obtained for pure O_2 and 12 per cent O_2, respectively.

These experiments were carried out in eight subjects and the mean n-values were found to be 2.274 (1.980-2.520) and 2.165 (1.945-2.310) for O_2 and air, respectively. The corresponding value for breathing 12 per cent O_2 was equal to 1.866 (1.530-2.260). By considering that in healthy subjects a difference in the O_2 saturation of about 2.5 per cent exists when breathing pure O_2 or room air, and that when breathing 12 per cent oxygen the mean value of the oxygen saturation determined with the oximeter in the course of these experiments was found to be 80.4 (69-92) per cent, it becomes apparent from the results that the n-value for air follows closely that obtained for pure O_2 and is very different from that obtained for 12 per cent O_2. These results may be presented in the following way: assuming that the mean value for $n = 2.274$ indicates that 40 per cent of the incident light was transmitted through the pinna, when pure O_2 was breathed, then $n = 2.165$ and $n = 1.865$ indicate that the transmission was 38 and 32.8 per cent for breathing air and 12 per cent oxygen, respectively.

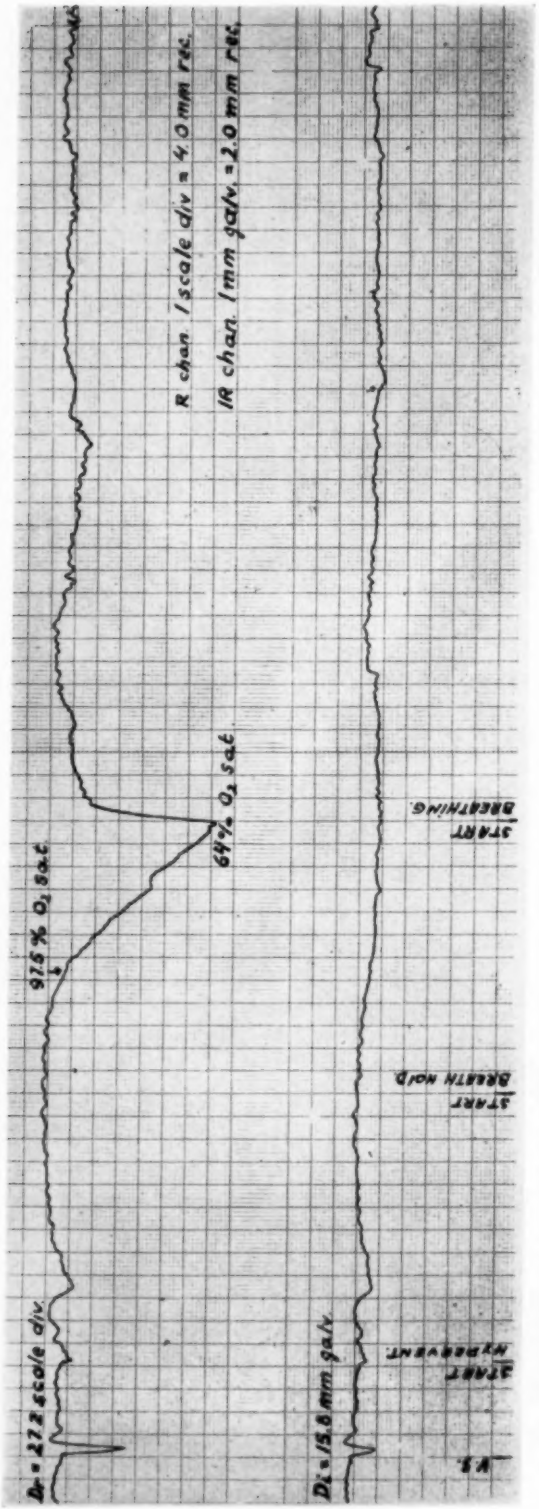
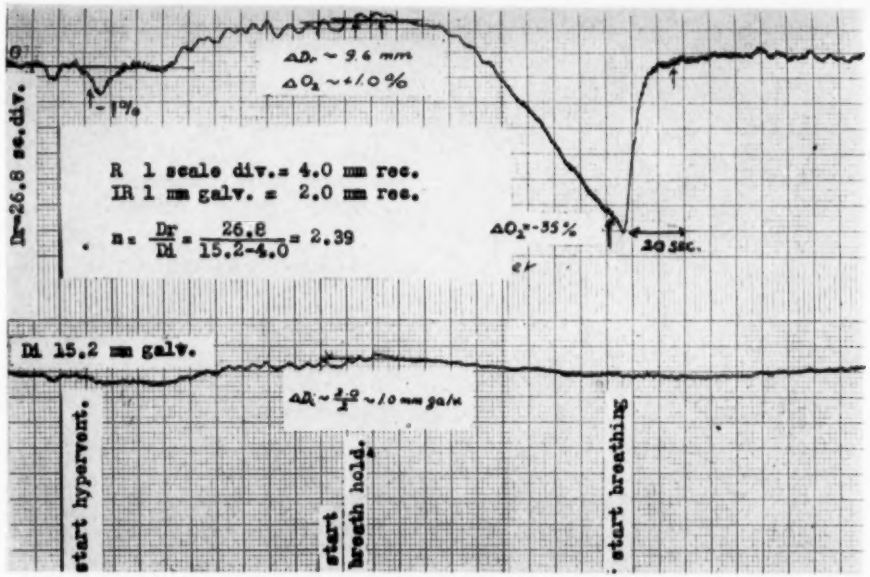


Fig. 9A.—Record of breath-holding following hyperventilation on room air in subject A.G. Note marked changes in the infrared transmission.

Segment 1. →



Segment 2.
↓

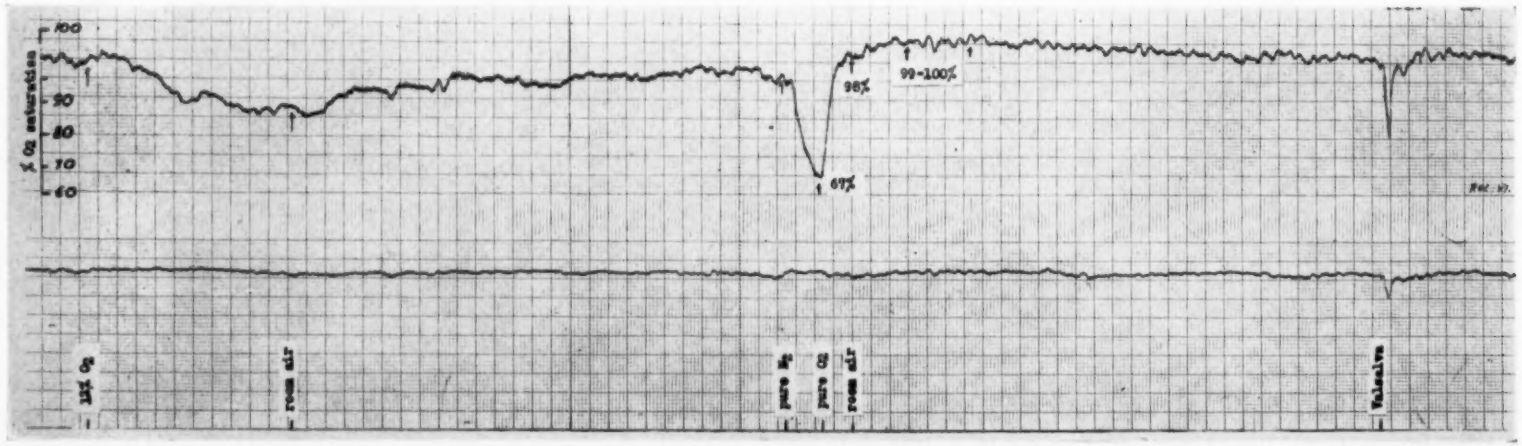


Fig. 9B.—Segment 1, Record of breath-holding following hyperventilation on room air in subject A.G. Segment 2, Record of changes in the oxygen saturation in the same subject when breathing different gas mixtures. Marked changes in infrared transmission may be observed.

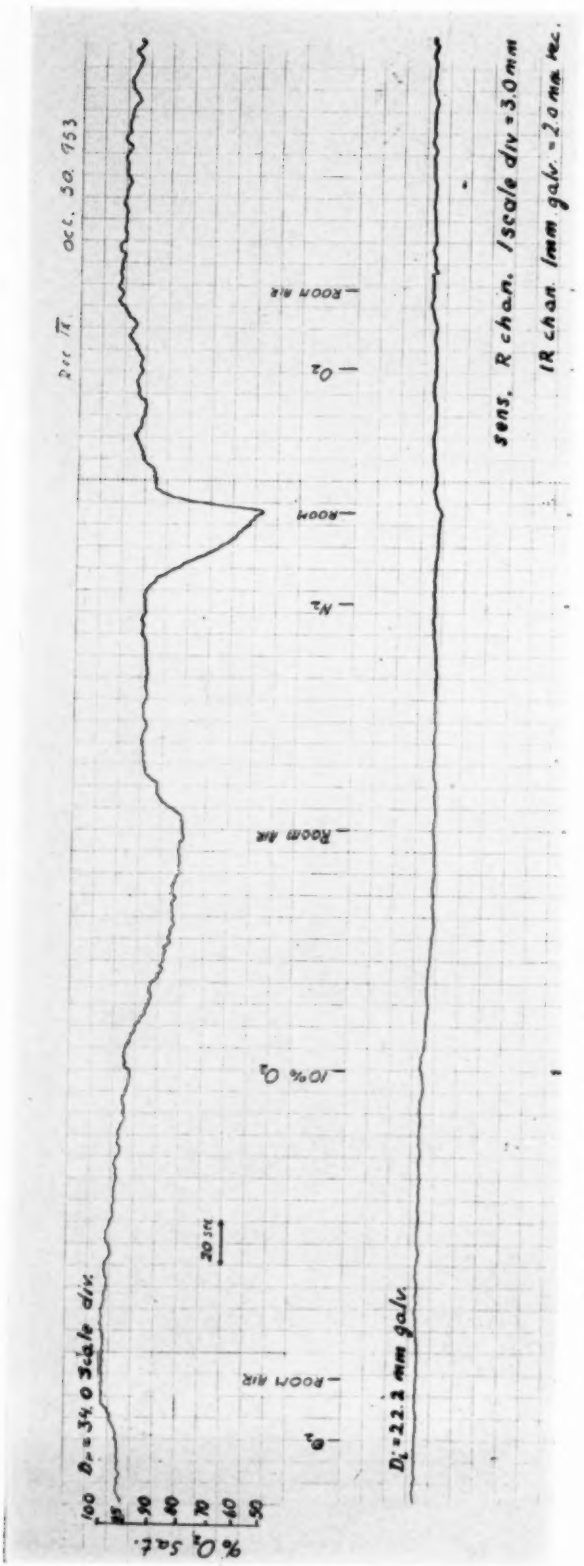


Fig. 10.—Record of red and infrared transmission obtained in subject P.S. breathing different gas mixtures.

The ratios for the per cent oxygen saturation and for the calculated transmission for the three gases appear to be in good agreement, as indicated by 100:97.5:80—40:38:33.

In spite of the fact that no gas analytical determinations on simultaneously drawn blood samples were performed, the results seem to indicate that the blood in the heat-flushed pinna must have had an oxygen content comparable to that contained in the main arteries.

Saturation Time Measurements.—To re-examine whether the oximeter using radiant heat to flush the ear provides reliable measurements of time in studies on circulation and on lung functions, experiments were carried out in healthy subjects under varying respiratory activity.

Sample records (Figs. 9 to 13) show the rate at which the oxygen saturation and "ear-thickness" change under varying respiratory activity. Fig. 9A is a record of breath-holding following hyperventilation on room air. Before the start of the hyperventilation the subject was required to perform the Valsalva experiment. Following this, both the R and IR lines remained slightly below base-line levels indicating that the vasodilatation achieved at the start of the experiment was not quite adequate.

During hyperventilation a gradual increase in the light transmission was recorded with both channels indicating a rise in oxygen saturation and a simultaneous vasoconstriction. This vasoconstriction caused an apparent increase in the oxygen saturation. During breath-holding the oxygen saturation first remained constant, then decreased slowly and finally more rapidly at a uniform rate. With onset of respiration the oxygen saturation increased at first very rapidly then more gradually to reach room air level in 30 seconds. Following this the respiration was irregular in depth and rhythm causing the oxygen saturation to fluctuate by as much as ± 1 per cent. Vasodilatation, as indicated by a decrease in the IR line, appeared soon after, and eventually reached a maximum towards the end of breath-holding. Blood volume changes, if not accounted for, would have caused errors of about + 2.0 and − 7.0 per cent in the estimation of the arterial oxygen saturation, at the highest and the lowest levels, respectively. Because of the marked variations in the IR readings observed in this subject, it was decided to repeat the experiment. The result obtained is shown in segment 1 of a long record reproduced in Fig. 9B. The general aspect of this record is similar to that previously obtained. The vasoconstriction and apparent increase in the oxygen saturation were more pronounced than in the previous record. Variations in both light transmissions, in phase with the respiration during hyperventilation, are clearly seen. Vasodilatation occurring during breath-holding was less marked than previously. With the onset of breathing the oxygen saturation returned to the base-line level in 24 seconds and reached a constant plateau in 48 seconds. Segment 2 of the same record shows a slow, irregular decrease in the oxygen saturation with the subject breathing 12 per cent O_2 and a very slow recovery upon changing to room air. When the breathing mixture was changed from air to N_2, the oxygen saturation in the subject fell very steeply after two to three breaths of this gas, and then rose, following the inhalation of three breaths of O_2, to reach the 98 per cent level in 16 seconds and

equilibrium in 45 seconds. Minor fluctuations not greater than 0.5 per cent about this plateau were observed. It took nearly 4 minutes for the oxygen saturation to return to the room air level after the inhalation of three breaths of O_2. The Valsalva experiment was carried out as a final check on the constancy in the R and IR deflections with the subject breathing room air.

Fig. 10 shows the records obtained in a subject breathing different gas mixtures. Upon changing from room air to pure O_2 the oxygen saturation reached a constant plateau in 18 seconds and it then took 140 seconds for the oxygen saturation to return to room air level when the subject was changed from O_2 to air. Upon changing from air to 10 per cent O_2 the saturation fell slowly and it rose in 40 seconds to base-line level on changing from 10 per cent O_2 to air. When breathing pure N_2 the oxygen saturation decreased steeply and returned in 24 seconds to base-line level on changing from N_2 to air. Upon changing from air to pure O_2 the saturation reached a maximum value in 28 seconds. If the variations in the IR readings had been neglected, an error of -1.5 per cent at the level of 80 per cent, and -4.5 per cent at the level of 58 per cent oxygen saturation would have resulted in the oximeter readings.

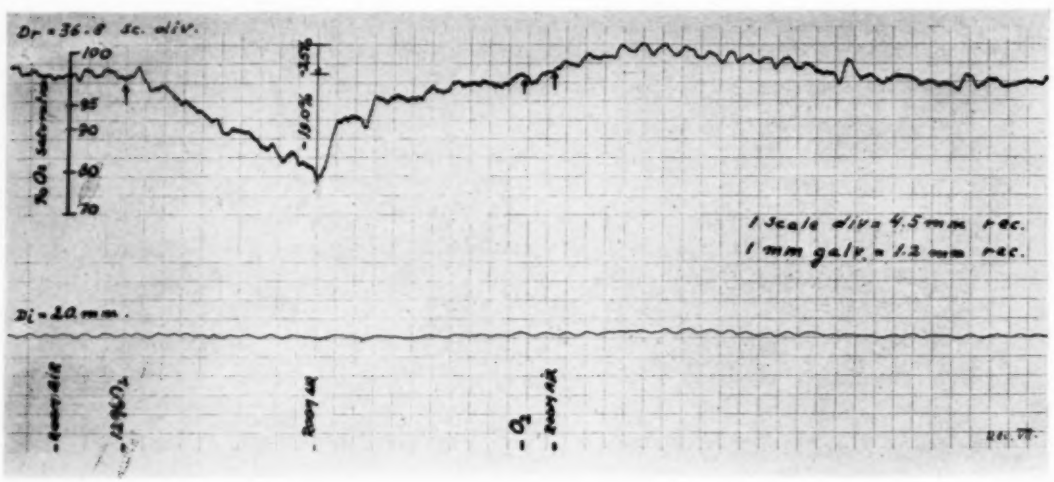


Fig. 11.—Record of changes in the oxygen saturation and ear-thickness obtained in subject A.L. breathing different gas mixtures. Increase in the infrared transmission indicated vasoconstriction when pure O_2 is breathed.

The sensitivity of the recording oximeter to depict fine details may be illustrated by the tracing shown in Fig. 11. Here, the arterial oxygen saturation decreased along a straight line, with the subject breathing 12 per cent O_2, and returned in a somewhat irregular manner to the base-line level on changing to air. Fluctuations in the recorded oxygen saturation were due to irregularity in respiratory rate and depth. Two breaths of O_2 following room air breathing caused the oxygen saturation to rise and apparently to reach the maximum plateau in 52 seconds. The upward movement of IR-stylus indicated vasoconstriction which appeared soon after the inhalation of the O_2. This is believed

to have been caused by a slight degree of overbreathing and is similar in pattern to that observed when subjects were hyperventilated on room air. Similar observations were made in a few other cases as well and one of these is illustrated in Fig. 12. Here, after a forced Valsalva experiment, pure N_2 was breathed and three breaths of this gas caused a steep decrease in the oxygen saturation which returned to a level of 98 to 99 per cent in 20 seconds when the inhaled gas was switched from N_2 to O_2. While breathing O_2 for 120 seconds, both the R- and the IR-stylus continued to move upward, with a steadily diminishing rate, to reach maximum values in 132 seconds after the inhalation of the first breath of O_2.

If vasoconstriction occurs while pure O_2 is breathed, following inhalation of room air or of a low O_2 mixture, it becomes apparent that the records indicate an increase in the time required by the hemoglobin to attain full saturation. Under these conditions considerable error may be produced in the estimations of the resaturation time of the hemoglobin with the oximeter, which does not provide adequate compensation for changes in blood volume.

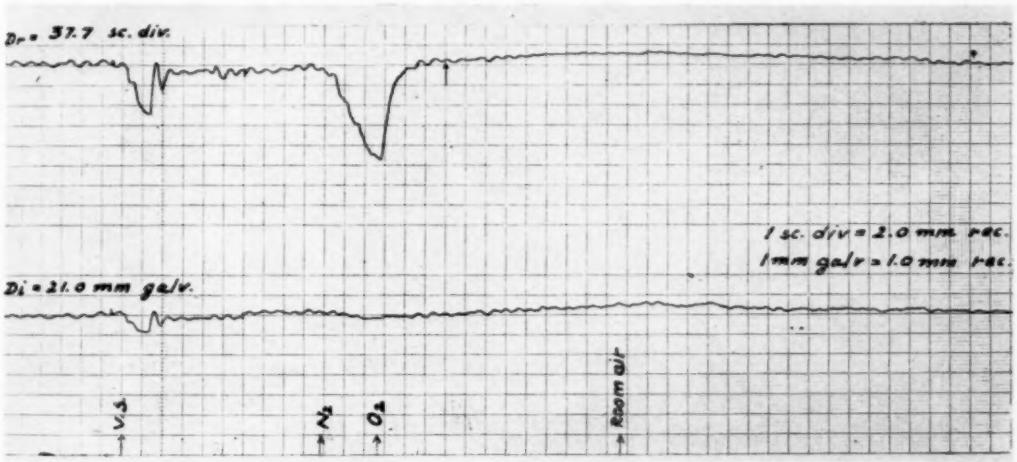


Fig. 12.—Record obtained in subject D.C. breathing different gas mixtures. Marked vasoconstriction may be observed during inhalation of pure O_2.

Saturation times which were observed in eleven subjects are shown in Table III. Column a contains the times in which the oxygen saturation reached a maximum plateau on changing the subjects from air to pure O_2: columns b and c the times in which the saturation attained base-line level and maximum plateau, respectively, on changing from below 80 per cent saturation to pure O_2. It should be noted that the term "maximum plateau" is used here to denote the mean value of the maximum elevation about which small fluctuations in phase with the respiration may occur.

From results shown in Table III it appears that vasoconstriction was observed in three out of eleven subjects examined, while they were breathing pure O_2. Considerable apparent prolongation of the saturation time was ob-

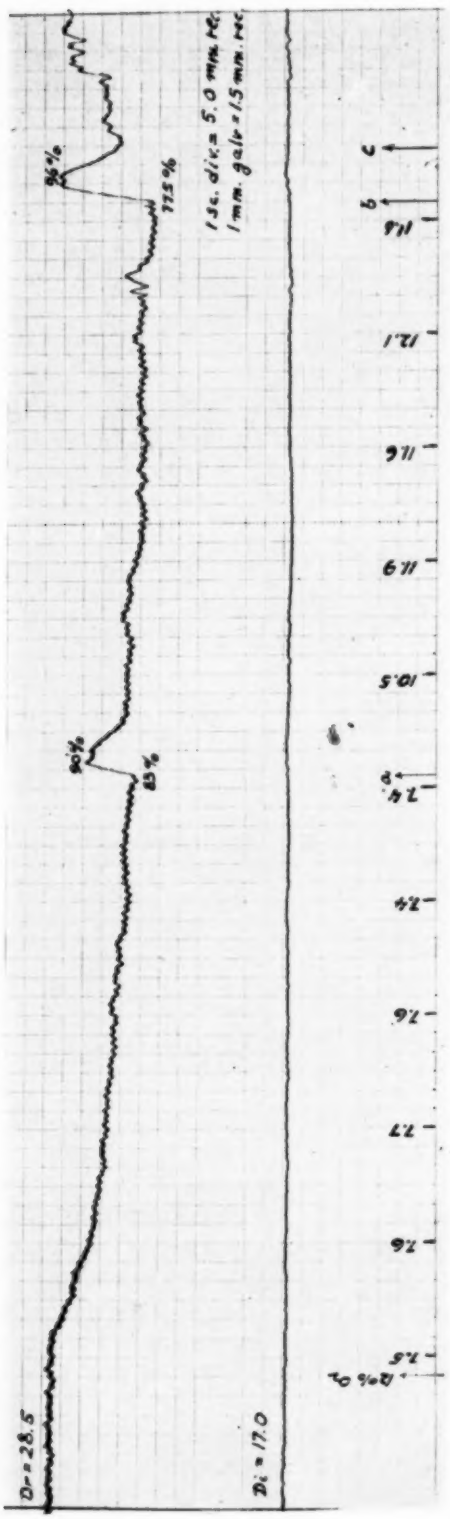


Fig. 13.—Record of an experiment to determine the respiratory dead space with the oximeter in subject P.R. breathing 12 per cent O_2. At points *a* and *b* sudden increase in the tidal volume produced considerable increase in the oxygen saturation.

TABLE III

RECORD NO	RESATURATION TIME IN SECONDS			VASOCONSTRICTION OBSERVED
	a	b	c	
VI	—	16	30	Slight
IX	20	—	—	No
	28	—	—	No
X	—	30	14	No
VII	—	18	68	Marked
V	—	20	112	Marked
IV	—	16	70	No
III a	—	26	40	No
III b	—	18	12	No
XI	24	18	20	No
XII	—	22	16	No
XIII	26	24	28	No
XIV	18	24	12	—
XV	52	—	—	Marked

served in the two cases when the vasoconstriction was the most marked. The approximate mean values in seconds for columns a, b, and c were found to be: 28 (18-52), 21 (16-30), and 38 (12-112), respectively. These results are essentially in good agreement with those obtained by others. For instance, Wood and associates[6] with the Wood oximeter found the following values corresponding with those recorded above: 47 (19-74), 19 (14-28), and 25 (11-58). The difference between the values in column c, Table III, and the corresponding values obtained by Wood, may be explained by the fact that he has taken the plateau value minus 0.5 per cent as a limit, as did Fowler and Comroe[7] in the lung-function studies carried out with the Millikan oximeter.

Although the experiment, the record of which is shown in Fig. 13, is not pertinent to the questions examined above, its inclusion in this section may appear to be of interest because it seems to be relevant to some observations made in the course of the foregoing experiments. For example, it was a surprise to observe the oxygen saturation stabilizing at a level of about 92 per cent in a subject after prolonged inhalation of 12 per cent oxygen. It was believed that a slight degree of overbreathing of this gas mixture may explain this observation. In the experiment to be presented, an attempt was made to determine the respiratory dead space from the difference in the tidal volumes in a subject in whom the arterial oxygen saturation was maintained at a constant level while breathing 12 per cent oxygen first from a Douglas bag through a mouthpiece only,

and then through an added "dead space" in the form of a corrugated respiratory tubing. It was found that the dead space determined in this manner corresponded reasonably well with that obtained in the same subject from oxygen saturation values determined with the Haldane apparatus on alveolar samples.

On the record it will be noted that there was a slow, gradual decrease in the oxygen saturation in the subject while breathing this 12 per cent oxygen at a rate of 15 breaths per minute. The values of the minute volume, measured with a flow meter, are marked on the abscissa. At the point *a* the subject was required to take a deep breath and hold it for a very short time while the tubing was inserted into the "circuit." Note the very sharp increase in the oxygen saturation of 7 per cent with a single deep breath. Between points *a* and *b* the respiratory rate increased to 17 per minute and the minute volume showed an increase of about 50 per cent while the level of the oxygen saturation did not vary by more than about 5 per cent. At point *b* a sudden rise in the oxygen saturation to nearly room air level was produced with two deep breaths of this gas. At the point *c* the breathing mixture was switched to air; the breathing became irregular which caused the oxygen saturation to rise with marked fluctuations toward the base-line level.

This record appears to be a good illustration of the changes produced in the composition of the air in the alveoli and of the rate at which these changes take place when the tidal volume varies.

Compensation for Variations in "Ear-Thickness".—It was pointed out previously that the operation of this oximeter is partly based on separate, simultaneous readings taken with both red and infrared filtered photocells. The "ear-thickness" was defined by $d = \frac{2.3}{C_i - C_r} [\log D_r - \log (K \cdot D_r)]$, (Eq. 6a, p. 842),[1] and the relationship which exists between the output currents of both photocells defined by $D_r = n (D_i - a)$: combining these two expressions and rearranging the terms one obtains:

$$d = \frac{2.3}{c_i - c_r} \left\{ \log \left[n \left(1 - \frac{a}{D_i}\right) \right] - \log K \right\} \qquad (1)$$

where, it will be recalled, c_i, c_r, a, and K are constants. If it could be demonstrated that the value of n in the same subject is not altered by changes in the blood volume then d will be dependent on the only remaining variable, D_i.

In the course of the Valsalva experiments reported above, it was observed that when vasodilatation was maximum, increases of 3 to 5 per cent were produced in the n-values for corresponding decreases of about 12 to 16 per cent in the D_i-readings. One of these experiments is illustrated by the record shown in Fig. 14. Here, Subject D.C., Table III, performed the Valsalva maneuver after breathing pure O_2 for 5 minutes. Because changes of these magnitudes exceed by far those which normally occur in the clinical use of the oximeter, negligible errors in the estimation of the arterial oxygen saturation will result when the "ear-thickness" is computed from Eq. 1 in which n is considered as invariant in the same subject. On the average the effect of disregarding changes of the order

of ± 2 per cent in the n-values will produce an error in the determination of the arterial oxygen saturation within ± 1 per cent at a level of 70 per cent and within ± 2 per cent at the level of 50 per cent oxygen saturation.

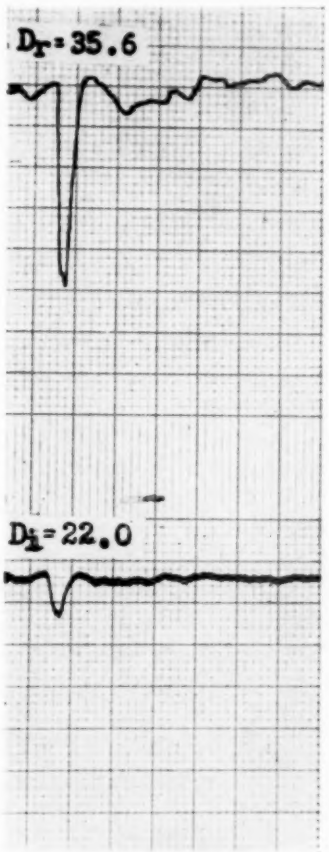


Fig. 14.—Record of the Valsalva maneuver performed by subject D.C. after inhalation of pure O_2 for 5 minutes. R chan. 1 scale div. = 5.0 mm. rec. IR chan. 1 mm. galv. = 2.0 mm. rec.

In practice, Eq. 1 is not used in the form shown because it is too cumbersome to operate with. Compensation for changes in the blood volume are obtained by introducing into the relationship $D_r = n\ (D_i - a)$ the value of D_i read directly off the galvanometer scale at any moment and setting the vertical scale cursor of the calculator in accordance with these values.

The above expression may be written in a more general form for changes occurring in the blood volume for either sign of ΔD_i

$$\Delta D_r = n\ (D_i \pm \Delta D_i) - na - D_r \qquad (2)$$

where ΔD_r is that fraction of the change in the deflection D_r which is due to changes, ΔD_i, in D_i. D_r and D_i refer to measurements taken at the beginning of the experiments.

In order to illustrate the manner in which changes in the "ear-thickness" are accounted for when using the direct-recording oximeter, sample calculations are presented.

Subject, A. L. Hyperventilation and breath-holding, see Segment 1, Fig. 9B.

Sensitivity of the recording system:

R channel . . . . . 1 scale div. = 4.0 mm. recorder defl.

IR channel . . . . . 1 mm. galv. defl. = 2.0 mm. recorder defl.

a. *Hyperventilation*

Measurements at the beginning of the experiment:

$D_r = 26.8$ scale divisions

$D_i = 15.2$ mm. galv. defl. = 30.4 mm. recorder defl.

$$n = \frac{26.8}{15.2 - 4} = 2.39$$

During hyperventilation the maximum change in D_i was

$$\Delta D_i \sim + \frac{2.0}{2} \sim 1.0 \text{ mm. galv. defl.}$$

In accordance with expression 2

$$\Delta D_r = 2.39\ (15.2 + 1 - 4) - 26.8 = 2.4 \text{ scale div.}$$

The maximum change in D_r observed during hyperventilation was equal to $\frac{11.5}{4} \sim 2.88$ scale divisions and the difference $2.88 - 2.4 = + 0.48$ scale div. was apparently caused by a change in the oxygen saturation. The per cent change in the oxygen saturation was found by using the calculator.

Set horizontal scale cursor to:

$R_1 = \log (D_r + \Delta D_r) = \log (26.8 + 2.4)$	=	1.465
$R_2 = \log (26.8 + 2.88)$	=	1.473
$R_1 - R_2$	=	−0.008

Set vertical scale cursor to:

R_1	=	1.465
$IR = \log (D_i + \Delta D_i) = \log (15.2 + 1)$	=	1.201
$R_1 - IR$	=	0.264

The rotating arm of the calculator indicates an increase of about 1 per cent in the oxygen saturation. The initial oxygen saturation in the subject while quietly breathing air was 98.0 per cent; during hyperventilation it increased to about 99.0 per cent. Disregard of the changes in D_i, due to vasoconstriction, would have made the value of the oxygen saturation to appear higher than 100 per cent.

b. *Breath-holding.*—Maximum change in D_i:

$$\Delta D_i \sim - \frac{1.2}{2} \sim 0.6 \text{ mm. galv. defl.}$$

$$\Delta R \sim 2.39\ (15.2 - 0.6 - 4) - 26.8 = -1.4 \text{ scale div.}$$

The maximum change in D_r due to decrease in the oxygen saturation below room air level was equal to the difference $\frac{32}{4} - 1.4 = 6.6$ scale divisions.

Set horizontal scale cursor of the calculator to:

$$R_1 = \log (D_r - \Delta D_r) = \log (26.8 - 1.4) = 1.405$$
$$R_2 = \log (26.8 - 8) = 1.274$$
$$R_1 - R_2 = 0.131$$

Set vertical scale cursor to:

$$R_1 = 1.405$$
$$IR = \log (D_i - \Delta D_i) = \log (15.2 - 0.6) = 1.164$$
$$R_1 - IR = 0.241$$

The rotating arm indicates a decrease of 35 per cent in the O_2 saturation. If changes in the D_i reading, due to vasodilatation, had not been accounted for, an error of about 5 per cent would have resulted in the estimation of the oxygen saturation.

When the direct-recording oximeter is used, because of the necessity to convert the recorder deflections in millimeter galvanometer deflections and scale divisions, the calculations appear somewhat laborious. However, the operation is much simpler than would appear due to the fact, as stated previously, that both the galvanometer and the dial are provided with linear and logarithmic scales. Thus no reference has to be taken to logarithmic tables or to slide rules. The calculations are reduced to a very minimum when the oximeter operates on the principle of a null-bridge method with the galvanometer serving as the null indicator. In this case all readings are directly taken on the dial and galvanometer scales.

COMMENTS

Increased accuracy and reliability in the determination of the arterial oxygen saturation were obtained with the oximeter when using the earpiece described above. Because of the small size of the earpiece it could be used successfully in very young children with practically no risk of earburn. Earpieces of this type have been used during the past two years in different places and on a great number of occasions, in subjects ranging in age from two weeks to that of adults. Only one case of a minor degree of earburn has been reported in a two-month-old child with tetralogy of Fallot, after an operation of several hours' duration. From the site of the burn, on the upper rim of the pinna it was concluded that the earpiece must have been improperly fitted and had slipped during the operation. Several cases of skin irritation were also observed in small children after prolonged operation.

With regard to the optical characteristics of the earpiece it may be stated that: (a) The choice of two layers of Wratten 87 filters made the infrared readings practically completely independent of the oxygen saturation. Whenever changes in these readings occur they are due only to changes in "ear-thickness." (b) Errors due to the presence of visible vessels in the vascular bed of

the pinna are greatly reduced by the arrangement of the optical system. In Fig. 2 it will be seen that the light source is located in a semicylindrical reflector about 20 mm. distant from the photocell housing. The reflector is made of Duralumin and has a mat-reflecting surface. Diffuse light emerging from this source passes through the pinna, and then through the glass-and-Lucite window and light filters to fall upon the photocells which are located 4 mm. away from the dorsal skin of the pinna. This arrangement appears to provide a simple and effective means of producing a considerable light scatter, thus assisting the elimination of sharp shadows of discrete vessels which may be cast on the photocells. Paul and associates[8] have carried out investigations to determine the error in oximetry due to vascular patterns in the ear and Taplin and associates[9] constructed earpieces in which optical means and multisection photocells were used to reduce this error. (c) Some decrease in the accuracy of the determinations and loss of sensitivity to changes in the oxygen saturation result from the utilization of light which is not sufficiently monochromatic. In the author's opinion little is to be gained in the practical use of the oximeter by too great an elaboration of an ideal optical system in the earpiece when the principal link in the chain, the pinna itself, is so optically imperfect. There can be no doubt that the specific sensitivity of the system would be increased by using, for example, interference filters with a narrow transmission band. Utilization of such means to provide monochromatic light at a greatly reduced light intensity would necessitate a considerable increase in the sensitivity of the galvanometer and the final result would be a much more delicate and unstable operation. Where direct-writing recording is required, however, and amplifiers with sufficiently high gain, stability, and good linearity are available, a somewhat increased accuracy may be expected by the use of monochromatic light filters in the earpiece.

The agreement between the results obtained with the oximeter and those on simultaneously withdrawn arterial blood samples analyzed by the Van Slyke method was better in healthy adults than in children with cardiovascular defects. It has been pointed out previously that much of the total error is due to sampling difficulties in small children. The standard deviation of the differences in per cent oxygen saturation between the values determined with the oximeters and those obtained by the Van Slyke method of analysis in the range from 48 to 100 per cent oxygen saturation was found to be 2.00 in adults and 2.65 in children with suspected hypoxemia. In spite of this observed variability in the accuracy for these two groups, the results seem to indicate that the absolute value of the oxygen saturation can be determined in adults as well as in children with arterial unsaturation with an adequate degree of accuracy without the necessity to preset the instrument to known values of arterial oxygen saturation.

The results obtained with five individual oximeters and earpieces preset with optical filters, all having nearly identical calibration lines, indicate that one of the chief disadvantages of the oximeter as a practical tool, namely, the necessity to calibrate each individual earpiece by comparison with gasometric determinations, has apparently been overcome.

A practical advantage results from the fact that only two readings at any moment are required to compute the value of the arterial oxygen saturation by

means of the calculator. This is made possible by the circuit arrangement. In this manner the necessity to use logarithmic tables or slide rules and to consult calibration diagrams is eliminated.

Evidence for adequate "arterialization" of the blood in the vessels of the pinna was obtained in experiments with the direct-writing oximeter. This factor may be disregarded as a major source of inaccuracy in the oximetric determinations of the arterial oxygen saturation. Our observations seem to agree with those made by Lilienthal and Riley[10] who demonstrated that the blood obtained by puncture of the ear lobe following application of radiant heat to the ear was essentially arterial. It should be pointed out, however, that in some subjects complete stability in the IR readings was not achieved even after prolonged flushing of the pinna. Observations over a period of several hours indicated that an extremely slow, steady increase in vasodilatation did occur in some cases. As the ratio of the red to the infrared readings was not altered, or only to an insignificant degree in these subjects, it is believed that the accuracy of the oximetric determinations by this method will not be significantly affected by this factor.

The principal disadvantage of the oximeter described is that the values of the arterial oxygen saturation cannot be directly read off a scale but have to be converted from two separate readings with the help of the calculator. This is necessary because the circuitry does not provide automatic compensation for changes in the blood volume. In the writer's opinion adequate compensation for these changes, hence good accuracy in the determinations, cannot be achieved by using a single-scale arrangement, but double-scale operation, based on simultaneous separate readings of the output currents of both photocells appears to provide reasonably simple and satisfactory operation. Automatic compensation for changes in the blood volume is considered to be a problem for an electronic computer. Such an instrument is in an advanced stage of development in this laboratory.

SUMMARY

An improved earpiece, a built-in two-beam galvanometer, and a calculating device for the photoelectric determination of the arterial oxygen saturation in man by means of the oximeter are described. Absolute determinations of the oxygen saturation with the oximeter preset with optical filters are presented. A direct-writing recording oximeter is briefly described. Indirect methods to investigate the adequacy of the "arterialization" of the capillary blood by radiant heat of the light bulb of the earpiece and oxygen saturation time measurements are reported. Methods for compensation of changes in "ear-thickness" are discussed.

The writer is much indebted to Drs. F. C. McIntosh and A. S. V. Burgen, Department of Physiology, McGill University, for helpful discussions. To the following members of The Children's Memorial Hospital: Dr. A. L. Johnson, for his helpful co-ordination and to Dr. C. Ferencz, who performed the arterial punctures, he expresses his sincere appreciation; the secretarial assistance of Mrs. I. Cloutte and Miss A. M. Pratt is gratefully acknowledged.

REFERENCES

1. Sekelj, P., Johnson, A. L., Hoff, H. E., and Pratt Schuerch, M.: Photoelectric Method for the Determination of Arterial Oxygen Saturation in Man, Am. Heart J. **42**:826, 1951.
2. Elam. J. O., Neville, J. G., Sleator, W., and Elam, W. W.: Sources of Error in Oxymetry, Ann. Surg. **130**:755, 1949.
3. Matthers, K.: Untersuchungen Über den Gasaustausch in der Menschlighen Lunge. I. Mitteilung. Sauerstoff Gehalt und Sauerstoff Spannung im Arterienblut und im Venösen Mischblut des Menschen, Arch. exper. Path. u. Pharmakol. **181**:630, 1936.
4. Hartman, F. W., Behrmann, V. G., and Chapman, F. W.: A Photoelectric Oxyhemograph. A Continuous Method for Measuring the Oxygen Saturation of the Blood, Am. J. Clin. Path. **18**:1, 1948.
5. Perkins, J. F., Jr., Adams, W. E., and Livingstone, H.: The Conversion of Millikan and Wood Type Oximeters Into Direct-writing Recording Instruments for Use in Surgery, in Studies of Pulmonary Function, and in Teaching Respiratory Physiology, J. Lab. & Clin. Med. **40**:457, 1952.
6. Wood, H. E., Taylor, B. E., and Knutson, J.: Oximetric Measurement of Circulation Time and Arterial Saturation Time During Oxygen Breathing in Man, Fed. Proc. **8**:171, 1949.
7. Fowler, W. S., and Comroe, J. H., Jr.: Lung Function Studies I. The Rate of Increase of Arterial Oxygen Saturation During Inhalation of 100% Oxygen, J. Clin. Invest. **27**:327, 1948.
8. Paul, W., Grapes, B. G., and Taplin, R. H.: Vascular Patterns in Ear as a Source of Error in Oxymetry, Fed. Proc. **11**:119, 1952.
9. Taplin, R. H., Saville, H. G., and Paul, W.: Improved Earpieces for Oximeters, J. Aviation Med. **24**:70, 1953.
10. Lilienthal, J. L., Jr., and Riley, R. L.: On Determination of Arterial Oxygen Saturations From Samples of "Capillary" Blood, J. Clin. Invest. **23**:904, 1944.

ACTION OF TRIETHANOLAMINE TRINITRATE IN ANGINA PECTORIS

DALE G. FRIEND, M.D., JAMES P. O'HARE, M.D., AND HAROLD D. LEVINE, M.D.

BOSTON, MASS.

EVER since the introduction of amyl nitrite for the treatment of angina pectoris by Brunton in 1867,[1] there has been a steady search for more effective agents for the relief of this affliction. This has been based on the continuing hope that something may be found which will favorably affect the course of the underlying coronary arterial disease. Numerous substances have been studied, and the literature is redundant with claims and counterclaims for various compounds reputed to bring about coronary arterial dilatation with subsequent amelioration of the angina pains. The xanthines have been studied thoroughly by competent investigators, but after long periods of observation and employment of ingenious methods of evaluation, there is still no satisfactory answer to the question of their value in the treatment of coronary artery disease.[2,3] More recently, the same controversy has arisen concerning the Egyptian drug, khellin, which was carefully evaluated by two independent groups of excellent investigators, who came to exactly opposite conclusions about the efficiency of the agent.[4,5] Undoubtedly, much of this difficulty is due to the nature of the underlying coronary arterial lesion. The majority of patients coming to post mortem with fatal myocardial infarction show atheromatous change located about 1.5 cm. from the coronary orifice. It is not likely that such individuals would have responded to a coronary artery vasodilator in the same fashion as those with diffuse atheromatous lesions throughout many of the coronary arterial ramifications. It is conceivable that the results observed in any study could be considerably influenced by the topography of the disease process. As yet, there is no known way of determining accurately to which group a given individual with angina pectoris may belong. Furthermore, attacks of anginal pain can be precipitated by so many factors that it is most difficult to establish any real standard for measurement.

It is possible, however, that an effective coronary vasodilator would be helpful in coronary arterial disease if it could contribute to the development of increased collateral circulation. Theophyllin, khellin, and several nitrites show excellent coronary artery dilation in animal studies, but so far in men they have proved to

From the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Medicine, Harvard Medical School, Boston, Mass.

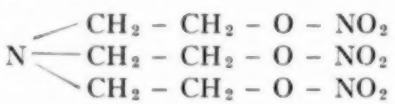
This work was supported in part by a grant from the Smith, Kline & French Laboratories, Philadelphia, Pa.

Received for publication May 21, 1954.

be of doubtful value in improving coronary artery disease. All produce undesirable side actions. Consequently, the search continues for newer and better agents with the hope that a highly effective, nontoxic, inexpensive one may be found.

Much study has been devoted to the nitrites and nitrates in the search for an effective, long-acting preparation, free of serious side reactions and to which little or no tolerance developed. The extensive studies of Krantz in this field resulted in the development of octyl nitrite, a new, useful preparation, which, however, has not received widespread acceptance clinically.[6]

Recently, interest has been shown in triethanolamine trinitrate, and several favorable reports have appeared indicating that this nitrate is a useful preparation in the treatment of angina pectoris.[7,8] It has the following chemical structure:



Triethanolamine trinitrate

This substance was first studied in Germany[9,10] and was considered to be of value in the treatment of angina pectoris. In view of the favorable reports on this agent, it was decided to evaluate its action in a few carefully selected patients.

METHOD AND MATERIAL

In recognition of the numerous pitfalls in a study of this type, every precaution was taken to make it as objective as possible. Seven patients were selected for study. They were individuals with typical anginal attacks. Most showed coronary artery disease, and all had experienced typical anginal attacks for at least a year. All of them took nitroglycerin for relief of their attacks.

The plan of study was to have patients continue on their usual program, taking nitroglycerin sublingually as needed for relief of attacks. Capsules containing 2.0 mg. of the drug, and two placebo agents, that is, capsules of lactose and capsules containing 2.0 mg. of nitroglycerin were given by mouth in a dose of one capsule before meals and at bedtime. Each drug was given for approximately one month (with some exception—R.S.), which made the study period nearly three months for each patient. This allowed ample time to compare the effect of triethanolamine trinitrate against that of the two placebos. Neither the patient nor the physician observing the patient knew which preparation was being taken. Patients were told that the drug received might be helpful, might be useless, or might even make them feel worse. Each patient was given a notebook in which he was to keep a daily record covering the following items: number of attacks, severity, whether they occurred at rest or with effort, frequency since taking last dose of drug, subjective evaluation of kind of day (good, average, or poor), and finally, any remarks he wished to make.

At the completion of the study, the notebooks were collected, the data assembled, and the key to the preparation received during any one period correctly assigned.

RESULTS

As is shown in Table I, there was no indication that triethanolamine trinitrate was any better than the placebos. It was well tolerated. No patient noticed any difference between any of the three agents given. It was also apparent that the capsules of nitroglycerin, given orally in a dose of 2.0 mg. four times a day, exerted no observable effect on the angina pectoris.

TABLE I

PATIENT	PLACEBO		TRIETHANOLAMINE TRINITRATE		NITROGLYCERIN	
	DAYS STUDIED	TOTAL NO. ATTACKS	DAYS STUDIED	TOTAL NO. ATTACKS	DAYS STUDIED	TOTAL NO. ATTACKS
H.E.D.	23	18	24	16	9	6
W.W.	32	48	31	60	26	59
L.A.G.	20	17	20	16	14	11
E.G.K.	33	36	37	28	27	27
R.S.	13	7	13	9	13	7
H.M.	29	18	30	24	26	20
P.K.	33	39	12	18	31	44

SUMMARY

1. Triethanolamine trinitrate in a dose of 2.0 mg., four times a day by mouth, is no better than a placebo in the treatment of angina pectoris.

2. Nitroglycerin, 2.0 mg., four times a day by mouth, was no better than placebo therapy.

3. Both triethanolamine trinitrate and nitroglycerin were well tolerated.

4. No toxic reactions were observed following both triethanolamine trinitrate and nitroglycerin given in a dose of 2.0 mg., four times a day by mouth, for periods of from two to four weeks.

CASE REPORTS

CASE 1.—H.E.D., a 60-year-old male was experiencing typical attacks of pain in the substernal area. Examination in the hospital showed early arteriosclerosis and an electrocardiogram characteristic of old myocardial infarction.

Following discharge from the hospital, he continued to have relatively mild attacks of angina on exertion such as walking to the office. He was given a placebo for twenty-three days, triethanolamine trinitrate for twenty-four days, and then a placebo for nine days. He could not detect any real difference between the three drugs received, although he did feel that he was somewhat less tired on triethanolamine trinitrate, but the difference was so slight that he could not be certain that it was not due to a better mental attitude on his part. He continued to have attacks throughout the three courses of therapy, and there were essentially no differences in the type of pain and frequency of attacks.

CASE 2.—W.W., a 73-year-old physician who has had angina pectoris for fourteen years. His heart is enlarged, and the electrocardiogram shows persistent changes of an old posterior myocardial infarction. For the past several years he has averaged eight to ten nitroglycerin tablets a day.

He was given a placebo for thirty-two days, following which he took triethanolamine trinitrate for thirty-one days, and then a placebo for twenty-six days. During this time he continued to have approximately two to three attacks of angina a day. As far as he could ascertain, there was no difference in his response to the three different capsules. Furthermore, he could observe no relationship between the time of appearance of attacks and taking of the capsules. He felt that he had not been benefited in any way by the course of therapy.

CASE 3.—L.A.G., a 57-year-old male who experienced a gradual increase in number of attacks until he could not take any exertion; even walking in his yard gave very severe angina. He has an elevated blood pressure, the heart is enlarged, and there is a Grade 4 systolic murmur at the aortic area transmitted to the neck. There was also a Grade 2 diastolic murmur in this area with obliteration of the second heart sound.

He was given a placebo for twenty days, triethanolamine trinitrate for twenty days, and a second placebo for fourteen days. During this entire time he continued to have almost daily attacks of angina pain and was unable to distinguish any difference between the drugs received, as far as his symptoms were concerned.

CASE 4.—E.G.K., a 60-year-old female with angina on exertion for six years. She exhibited early arteriosclerosis, and a Grade 3 apical systolic murmur is present. The electrocardiogram showed changes characteristic of old posterior myocardial infarction. She was experiencing daily pain from angina and had showed no improvement on any type of regimen. Triethanolamine trinitrate was started in a dose of 2 mg. before each meal and at bedtime. This was followed by placebo therapy. During all this time there was no improvement, and she continued to have pain on exertion. As far as she could ascertain, there was no real difference in the pain, and she could not detect any difference between the various capsules which she received during the three successive periods. She died of a fresh septal infarct in November, 1953.

CASE 5.—R.S., a 62-year-old female followed since 1936 for mild hypertension. Beginning in 1938 she experienced the onset of anterior chest pain. Since 1945 the chest pain had been very frequent on exertion and especially after eating heavy meals. The attacks were of typical angina and responded promptly to rest or nitroglycerin.

She was given a placebo for thirteen days, triethanolamine trinitrate for thirteen days, and another placebo for thirteen days. During this time she continued to have frequent attacks of pain and could not detect any difference between the drugs. She did express the opinion, however, that she felt better for a period on one of the drugs. When this was investigated it was found to be a placebo.

CASE 6.—H.M., a 55-year-old male who had suffered from typical attacks of anginal pain for the past two months. These were first noticed while he was exerting himself, but now they appeared even on rest or any slight exertion which was kept up for a few minutes. He had noticed that cigarettes apparently precipitated attacks. Examination showed a blood pressure of 135/90 mm. Hg, but there were no other abnormalities found. Laboratory findings were entirely normal. An electrocardiogram was also normal. He was placed on a placebo for twenty-nine days, triethanolamine trinitrate for thirty days, and then on a placebo for twenty-six days. During this time he continued to have as many attacks as previously, and he could notice no real difference between any of the drugs.

CASE 7.—P.K., a 59-year-old male who has typical attacks of angina pectoris. Nitroglycerin gives rapid relief of all symptoms. On examination he showed increased peripheral arteriosclerosis and a blood pressure of 150/90 mm. Hg.

He was given a placebo for thirty-three days, triethanolamine trinitrate 2.0 mg., four times a day, for twelve days, and a placebo for thirty-one days. He was unable to detect any difference in the number or severity of his angina attacks during these three periods.

REFERENCES

1. Brunton, T. L.: Use of Nitrite of Amyl in Angina Pectoris, Lancet **2**:97, 1867.
2. Gold, H., Kwit, N. T., and Otto, H.: Xanthines (Theobromine and Aminophylline) in Treatment of Cardiac Pain, J.A.M.A. **108**:2173, 1937.
3. Master, A. M., Jaffe, H. L., and Dack, S.: The Drug Treatment of Angina Pectoris Due to Coronary Artery Disease, Am. J. M. Sc. **197**:774, 1939.
4. Armbrust, C. A., Jr., and Levine, S. A.: The Treatment of Angina Pectoris With a Preparation of Khellin (ammi visnaga), Am. J. M. Sc. **220**:127, 1950.
5. Greiner, T., and others: A Method for Evaluation of Effects of Drugs on Cardiac Pain in Patients With Angina of Effort, Am. J. Med. **9**:143, 1950.
6. Krantz, J. C., Jr., Carr, C. J., and Forman, S. E.: Alkyl Nitrites II. The Pharmacology of 2-Ethyl-N-Hexyl-l-Nitrite, J. Pharmacol. & Exper. Therap. **64**:302, 1938.
7. Melville, K. I., and Lu, F. C.: Cardiovascular Effects of Triethanolamine Trinitrate, An Experimental Study, Canad. M. A. J. **65**:11, 1951.
8. Palmer, J. H., and Ramsey, C. G.: Triethanolamine Trinitrate (Methamine) in the Treatment of Angina Pectoris, A Preliminary Report, Canad. M. A. J. **65**:17, 1951.
9. Fischer, C.: Zur Behandlung der Angina Pectoris, Deutsche Gesundheitswesen **1**:455, 1946.
10. Pfeiffer, H.: Ueber die Wirkung von Trinitrat Auf den Menschlichen Kreislauf, Klin. Wchnschr. **28**:304, 1950.

THE COMPARATIVE DIURETIC EFFECTIVENESS OF MERCUMATILIN AND MERALLURIDE WITH AND WITHOUT CONCOMITANT ADMINISTRATION OF AMMONIUM CHLORIDE

ROBERT C. BATTERMAN, M.D.

NEW YORK, N. Y.

IN A previous communication[1] mercumatilin (Cumertilin) was reported to be a safe and effective diuretic which was well tolerated upon intramuscular injection. In contrast to experiences with other mercurial diurectics, it was noted with considerable surprise that the omission of concomitant administration of ammonium chloride with mercumatilin did not materially alter the likelihood of a satisfactory diuresis. Since the numbers of patients and of trials previously reported were small and did not lend themselves to statistical evaluation, it was thought advisable to extend this phase of the investigation. It is the purpose of this report, therefore, not only to present data confirming the original observation but also to indicate the general usefulness of mercumatilin when administered intramuscularly, intravenously, or orally for the treatment and control of congestive heart failure.

Since the effectiveness and safety of both mercurial diuretics used in this study have already been firmly established, our primary concern in this investigation was to duplicate as closely as possible the manner in which these diuretics are utilized by the general practitioner or by any hospital facility. For a period of two years, therefore, patients with congestive heart failure admitted to the cardiac service of the Bronx Veterans Hospital were followed for this purpose. If the status of the patient permitted, he was given either mercumatilin* or meralluride whenever a mercurial diurectic was required. The preparations, as a rule, were administered in 2 c.c. doses. With few exceptions, the patients had been previously digitalized by one of several digitalis preparations or glycosides and a daily dosage of the selected preparation continued throughout the period of observation. In all such patients this was the maximum tolerated dosage and was not by itself sufficient for removal or prevention of the reaccumulation of edema. The patients were given routinely a low-sodium diet, but this was also insufficient for adequate control of the signs and symptoms of the congestive heart failure. Many of the patients were in the terminal phase of their disease so that it was necessary in some in-

From the Department of Medicine, New York Medical College and Cardiac Section of the Medical Service, Veterans Administration Hospital, Bronx, N. Y.

Received for publication April 12, 1954.

*The author is indebted to Endo Products Inc. for the supply of the diuretic and other aid in connection with this investigation.

stances to supplement the effectiveness of the mercurial diuretic by the use of aminophylline. Only those trials in patients who were weighed daily are included in this report. If the patient was too ill to be weighed, either upon admission or subsequently, the responsiveness of the diuretic was not tabulated.

On any particular ward, only one diuretic was used for a period of three months and then the other diuretic substituted and used in identically the same manner as the previous one. There was thus no selection of patients in regard to which diurectic was to be used. The influence of concomitant administration of ammonium chloride was studied according to pure chance. If the patient had been receiving ammonium chloride before observation, it was continued with the same dosage schedule. In only a few instances was ammonium chloride specifically administered after the patient was included in the study. There was, therefore, no need except in these few instances for an additional control period for the effects of ammonium chloride alone to be evaluated. The dose ranged from one to two grams, three to four times daily, and was administered continuously or for three or four days before the mercurial diuretic was given.

A total of 134 patients was included in the investigation. Ninety-one patients received mercumatilin for a total of 458 trials. Seventy-three patients received meralluride for a total of 200 trials. Thirty patients were studied with both mercurial diuretics. Since the intramuscular route is the most popular at the present time, the majority of the patients were so treated. The number of injections ranged from one to forty, with the majority of the patients receiving three or more injections during their hospital stay.

TABLE I. EFFECTIVENESS OF MERCUMATILIN AND MERALLURIDE WHEN ADMINISTERED WITH AND WITHOUT AMMONIUM CHLORIDE

DIURETIC	CONCOMITANT ADMINISTRATION OF AMMONIUM CHLORIDE	NO. OF TRIALS	EFFECTIVENESS	
			NO. OF TRIALS	%
Mercumatilin	No	154	131	85.0
Mercumatilin	Yes	106	93	87.6
Meralluride	No	124	76	61.2
Meralluride	Yes	34	27	79.4

RESULTS OF PARENTERAL ADMINISTRATION

The effectiveness of mercumatilin and meralluride when given in 2.0 c.c. doses intramuscularly with and without the concomitant administration of ammonium chloride is presented in Table I. The concomitant administration of ammonium chloride was necessary to achieve a satisfactory diuretic response with meralluride but not with mercumatilin. For meralluride, the omission of ammonium chloride lowered the effectiveness of diuretic response from 79

to 61 per cent for a statistical significance* (Table II) of 3.04. For mercumatilin, an effective diuresis was obtained with and without ammonium chloride in 88 and 85 per cent, respectively. The responsiveness of mercumatilin without ammonium chloride as compared with meralluride without ammonium chloride indicated a high statistical significance of 11.5.

TABLE II. COMPARATIVE SIGNIFICANCE OF EFFECTIVENESS OF DIURETICS WITH AND WITHOUT CONCOMITANT ADMINISTRATION OF AMMONIUM CHLORIDE

	"*t*" VALUE*
1. Mercumatilin without ammonium chloride as compared with meralluride without ammonium chloride	11.5
2. Mercumatilin with ammonium chloride as compared with meralluride with ammonium chloride	0.86
3. Mercumatilin without ammonium chloride as compared with mercumatilin with ammonium chloride	0.61
4. Meralluride without ammonium chloride as compared with meralluride with ammonium chloride	3.04

*"*t*" value above 2.5 indicates significance.

For the advanced patient with congestive heart failure, mercumatilin administered in 2.0 c.c. doses intravenously was an effective and safe diuretic. The over-all responsiveness was approximately 85 per cent of thirty-five trials. For the patient who was no longer responsive to a mercurial diuretic regardless of route of administration, dosage, or concomitant use of ammonium chloride, then the additional simultaneous administration of aminophylline has proved to be an effective and safe means of initating a diuresis. In these far advanced patients, mercumatilin either intramuscularly or intravenously was used with aminophylline in thirty-one trials for an over-all incidence of effectiveness of approximately 77 per cent. Since prior to the use of aminophylline the patients were nonresponsive, this high incidence is of considerable significance.

The effectiveness and toxicity of mercumatilin administered orally were determined in eleven ambulatory patients with severe and progressive congestive heart failure. All patients were on the daily maximum tolerated dose of a digitalis preparation which was unable to control or prevent the reaccumulation of edema fluid. Mercurial diuretics administered parenterally at each clinic visit were required in all instances. Five of the eleven patients had previous experience with Mercuzanthin administered orally and had a satisfactory response to this form of therapy. Ammonium chloride in dosage of 1.0 Gm. three times daily was concomitantly given in six of the eleven patients. The diet was limited in salt but not salt poor.

*Statistical significance was determined by the Student "*t*" method. Values above 2.5 are significant.

Mercumatilin tablets* were given in doses of one or two tablets every morning. In those patients receiving oral Mercuzanthin, this diuretic was discontinued and mercumatilin substituted in its place. The duration of treatment varied from 3 to 37 weeks of continuous daily administration of mercumatilin tablets. Only three of the patients received the medication for less than eight weeks. One patient received the preparation for 37 weeks, while the others were observed from 25 to 29 weeks.

Two patients treated for three and eight weeks, respectively, had complete control of edema and did not require parenteral mercurial diuretics during this period. Eight patients presented satisfactory control of their signs and symptoms of congestive heart failure so that the need for parenteral mercurial diuretics was decreased. The five patients who had previous experience with oral mercuzanthin continued to have the same beneficial action with mercumatilin tablets. In only one patient who was treated for five weeks, was there an inadequate response to the tablets of mercumatilin. In none of the patients was there any manifestation of gastrointestinal disturbance, gingivitis, or other evidence suggestive of mercurialism or irritation. Although the number of patients is small, our experience with other orally administered mercurial diuretics allows us to conclude that mercumatilin, when administered in this way, is satisfactory for the control of progressive congestive heart failure. It will decrease the need for injectable diuretics and maintain the patient on a more stable level since it decreases the rapidity of edema reaccumulation. This is in accord with other investigators.[2]

DISCUSSION

Mercumatilin is an effective and safe mercurial diuretic which possesses several properties that lend themselves to advantage for satisfactory clinical use. The versatility of its administration by various routes, parenterally as well as orally with a high degree of effectiveness for each method and with minimal undesirable untoward effects, classifies this mercurial diuretic as a very useful one for the treatment of edematous states. In this respect it differs from other mercurial diuretics which are limited in usefulness, as a rule, for a single route of administration. Mercumatilin, thus, allows the physician a greater flexibility by the use of a single mercurial diuretic for the treatment of many problems encountered in patients with congestive heart failure.

It is now generally accepted that concomitant administration of acidifying salts is essential to obtain maximum predictability and responsiveness of the patient to a mercurial diurectic. In our previous studies[3] with other mercurial diuretics, the omission of ammonium chloride was a major factor for lack of diuretic response by the patient. This report emphasizes this factor in the case of meralluride. Without ammonium chloride, the administration of meralluride resulted in a diuresis in 61 per cent of the trials as compared with 79 per cent of the trials when ammonium chloride was given simultaneously. The statistical analysis is indicative of the significance of these results. On the other hand,

*Each tablet contained 67 mg. mercumatilin, equivalent to 20 mg. each of mercury and theophylline.

the results with mercumatilin indicate that the concomitant administration of ammonium chloride is not necessary to achieve a predictable and adequate diuresis. This unusual property of mercumatilin is therefore a decided advantage in favor of this preparation. Not only is it unnecessary to prescribe an additional medication which may produce gastrointestinal irritation in many patients, but also, the physician is assured that the usual patient will present as satisfactory a response to the diuretic whenever it is given.

SUMMARY AND CONCLUSIONS

1. Mercumatilin (Cumertilin) is an effective and safe mercurial diuretic which may be administered parenterally or orally.

2. Mercumatilin and meralluride were compared as to effectiveness with and without concomitant administration of ammonium chlorides.

3. The incidence of effective diurectic response with meralluride decreased from 79 to 61 per cent when ammonium chloride was omitted.

4. An effective diuresis was obtained with mercumatilin with and without ammonium chloride in 88 and 85 per cent of the trials, respectively.

5. Statistical analysis is indicative of the high degree of significance for the effectiveness of mercumatilin as compared with meralluride when administered without ammonium chloride.

6. The data confirm the conclusion noted previously[1] that the concomitant administration of acidifying salts is not essential for a satisfactory diuresis with the use of mercumatilin as with the use of meralluride and other mercurial diuretics.

REFERENCES

1. Rose, O. A., Lhowe, J., and Batterman, R. C.: Mercumatilin (Cumertilin): A New Mercurial Diuretic for the Treatment of Congestive Heart Failure, AM. HEART J. **40**:779, 1950.
2. (a) Pollock, B. E., and Pruitt, F. W.: Oral Therapy With Mercumatilin (Cumertilin): A New Mercurial Diuretic, Am. J. M. Sc. **226**:172, 1953.
   (b) DeGraff, A. C.: Personal communication.
   (c) Dimitroff, S. P., Lewis, R. C., Thorner, M. C., Field, J. B., and Griffith, G. C.: Oral Mercurial Diuretics—Mercumatilin, in the Treatment of Congestive Heart Failure, (submitted for publication).
3. (a) DeGraff, A. C., Nadler, J. E., and Batterman, R. C.: A Study of the Diuretic Effect of Mercupurin in Man, Am. J. M. Sc. **191**:526, 1936.
   (b) Batterman, R. C., Unterman, D., and DeGraff, A. C.: The Subcutaneous Administration of Mercaptomerin (Thiomerin), J.A.M.A. **140**:1268, 1949.
   (c) Batterman, R. C.: The Treatment of Congestive Heart Failure With Mercurial Diuretics, Medical Clin. N. A. **34**:629, 1950.
   (d) Batterman, R. C.: The Status of Mercurial Diuretics for the Treatment of Congestive Heart Failure, AM. HEART J. **22**:311, 1951.

THE SINUATRIAL NODE IN THE RAT

T. SUMMERFIELD KING, M.B., CH.B.

SHEFFIELD, ENGLAND

IN a recent paper by Prakash,[1] the statement appears that the sinuatrial (S-A) node is absent in the rat. But Keith and Flack,[2] the discoverers of the mammalian S-A node, found the presence of "pale staining fibres closely resembling those of the sinus of the frog" to be "remarkably constant" in their series of mammals which included the rat, and Meiklejohn,[3] though she gave no details of the structure of the node in the rat, indicated its position in her figures.

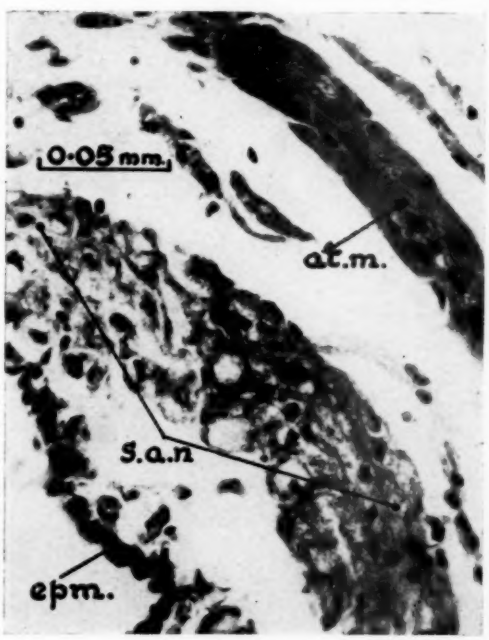


Fig. 1.—Photomicrograph of the sinuatrial node lying in the atrial wall of the rat.

In serial sections of the rat's heart prepared by the present writer there is a definite S-A node lying across the sulcus terminalis at the cranial extremity of the right atrium. This node consists of a bundle of fibers parallel to the epicardium, to a large extent separated from the ordinary atrial muscle by very delicate connective tissue containing numerous capillary blood vessels. Most of the faintly

From the Department of Anatomy, University of Sheffield, England.
Received for publication May 22, 1954.

cross-striated nodal fibers are broader than the ordinary atrial myocardial fibers and resemble Purkinje fibers but contain a number of coarse myofibrils. The nuclei are oval and mostly rather dark stained, though some are pale; they are surrounded by wide clear cytoplasmic zones. The whole structure resembles that in the ferret. The nodal artery pierces the fiber mass. Many of the nodal fibers are quite slender, and the node is connected to the ordinary atrial muscle by fibers of this type. Numerous nerve cells and nerve bundles lie alongside the node.

Histologic study of the hearts of a variety of mammals shows that while there are differences in the extent, shape, and details of histologic structure between the S-A nodes of these animals, there is an underlying similarity. The illustration shows the S-A node (*s.a.n.*) of a rat lying between the epicardium (*epm.*) of the sulcus terminalis and the atrial muscle (*at.m*).

REFERENCES

1. Prakash, Ravi.: Am. Heart J. **47**:241, 1954.
2. Keith, A., and Flack, M.: J. Anat. (Lond.) **41**:172, 1907.
3. Meiklejohn, J.: J. Anat. (Lond.) **48**:378, 1914.

Clinical Reports

ISOLATED MITRAL STENOSIS IN AN INFANT OF THREE MONTHS: REPORT OF A CASE TREATED SURGICALLY

G. M. MAXWELL, M.B., M.R.C.P., AND W. P. YOUNG, M.D.

MADISON, WIS.

ISOLATED congenital mitral stenosis is a rare condition. Cases are reported by Day,[1] Johnson and Lewes,[2] Emery and Illingworth,[3] and others. Surgery in two such cases has been reported by Bower and associates.[4]

This report describes such a case in an infant of three months. Mitral commissurotomy was performed at three and one-half months of age. The child survived for six weeks. The diagnosis and surgical result were confirmed post mortem.

CASE REPORT

This white baby girl was aged three months at the time of admission. She was the product of normal pregnancy and at delivery was seemingly normal. At the age of six weeks she began to breathe rapidly and had a 'wheeze.' Transient cyanosis was noted a few days before admission. A systolic murmur was heard.

Examination.—Weight, 4.4 kg.; length, 61 cm. The child showed poor nutrition with a grayish pallor. Hydration was normal. There was no clubbing or cyanosis. The breathing was rapid, with some indrawing of the lower intercostal spaces. There was no bulge of the chest. The peripheral pulses were normally palpable; the heart was enlarged to the left by inspection of the apex and percussion. A widespread systolic thrill was felt to the left of the sternum; auscultation revealed a loud systolic murmur, maximal at the mid-left sternal border, and widely transmitted to the right precordium, both axillae, and the interscapular area. The second pulmonary sound was loud but single. There was a constant triple rhythm over the displaced apex.

The blood count was normal apart from a moderate polymorph leukocytosis; electrolytes were normal, and serology was negative. The electrocardiogram showed Katz-Wachtel phenomenon, and evidence of vertical placement with clockwise rotation.

X-rays.—The heart was greatly enlarged (Figs. 1 and 2), with a huge left auricle displacing the barium-filled esophagus. The aorta was believed to be on the left, and the right ventricle was enlarged. The inner lung fields showed some increase in the vascular markings.

The provisional diagnosis (suggested initially by Dr. K. B. McDonough of the Department of Pediatrics) was fibroelastosis. As the child's condition was deteriorating, it was decided to carry out cardiac catheterization to exclude any associated defect.

The procedure was performed under Demerol analgesia via the left femoral vein. The child's condition was so perilous as to require continuous oxygen throughout, and this of course

From the Departments of Pediatrics and Surgery, University Hospitals, Madison, Wis.
Received for publication Feb. 6, 1954.

renders the blood oxygen levels unreal. Table I gives the results. The oxygen levels are remarkably constant, suggesting that no appreciable left-to-right shunt existed. Perusal of the pressure levels shows hypertension in the pulmonary capillary (wedge) portion, the pulmonary artery, and right ventricle. Hellems and associates[5] and Lagerlof and Werko[6] have demonstrated that

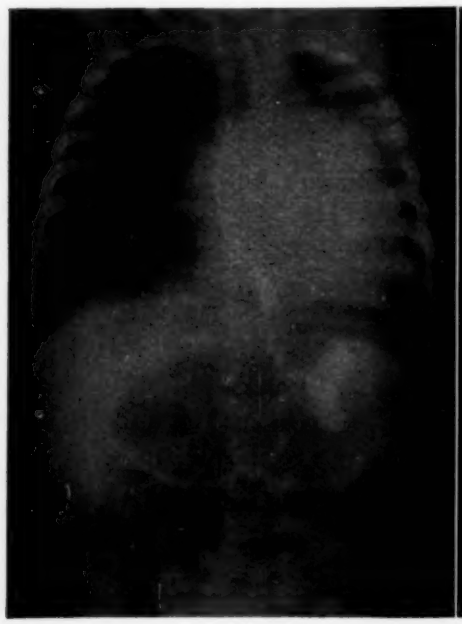


Fig. 1.

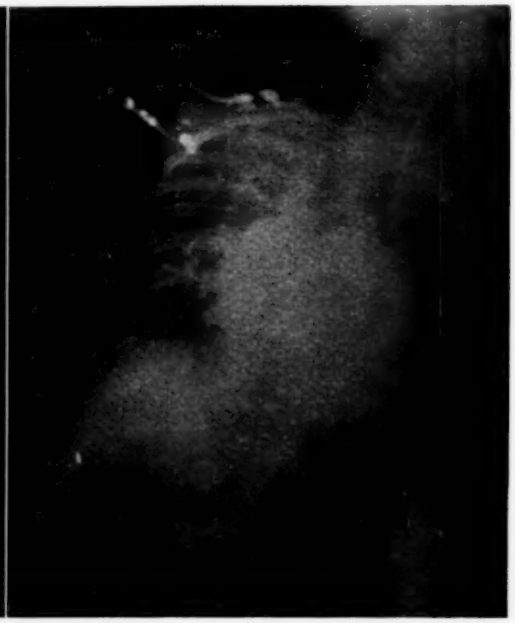


Fig. 2.

Fig. 1.—Anteroposterior view. The film shows great cardiac enlargement with displacement of the barium-filled esophagus by the left atrium.

Fig. 2.—Left posterior oblique position. This film shows the large left atrium by angiocardiography The difference in vascularity in the right and left lung fields is also visible.

TABLE I

CATHETER POSITION	PRESSURE MM. HG.	VOL. % OXYGEN
IVC	+0.1 (M)	7.14
SVC	+3.2 (M)	6.46
RA MID	−0.9 (M)	6.36
RV	50/−2.5	6.43
RPA	44.5/21.9 M = 34	6.52
RPA WEDGE	24.8/13.6 M = 18.8	
LPA	50/18.7 M = 34.5	6.63
FA	————	13.66
		Capacity 13.79

*M = Mean Hemoglobin 11.0 Gm.

the pulmonary capillary or wedge pressure accurately reflect the level in the left atrium, and in this case it was presumed that there was some condition raising the pressure in that chamber. Inspection of the pressure tracing taken in the wedge portion did not show the increased amplitude of the V wave coincident with ventricular systole which is considered by Gorlin and associates[7] to be suggestive of mitral regurgitation.

The conclusion from the physiologic study was that the results were consistent with, but not diagnostic of, mitral stenosis.

In view of the poor prognosis in the condition (Emery and Illingworth,[3] Blumberg and Lyon,[8] Freer and Matheson[9]), it was decided to carry out thoracotomy and attempt mitral commissurotomy. However, following the warning of Bower and associates[4] that the left ventricle and aorta should be well developed if surgery is to be successful, preliminary angiocardiography was carried out. This revealed (Fig. 2) a huge left atrium; there was no evidence of intracardiac shunt. It was noted that the filling of the right lung was less than that of the left. The aorta was unfortunately not well visualized. All evidence then pointed to a lesion of the left side of the heart which hindered atrial emptying, in accordance with the observation of Zinsser and Johnson.[10] By this time the child was more dyspneic, and the heart size (by x-ray) had increased. A short inconstant mid-diastolic murmur had appeared. The other signs were as before.

Thoracotomy was carried out when the child was just under four months old, and was preceded by digitalization.

Fig. 3.

Fig. 4.

Fig. 3.—The heart opened to show the left atrium, mitral valve and ventricle. The opaque endocardium of the left atrium is visible, as is the thickening of the left atrial and ventricular wall. The distortion of the mitral valve and short thick papillary muscles without obvious chordae are also visible.

Fig. 4.—The left atrium and mitral valve viewed from above. The mitral valve shows the thickened and wrinkled cusps. The line of commissurotomy stretches from four o'clock to ten o'clock. Note the thickened endocardium at the cut edge of the atrium.

Operative findings.—The heart was approached via a left infrascapular incision and was found to be very large; the left atrial appendage was much increased in size. A finger was introduced into the left atrial cavity, and the valve explored. The orifice would admit the fingertip only and was estimated to be about 1 cm. in diameter. A regurgitant jet was felt posteriorly, where the area of the commissure was thought to have a paper-thin but strong membrane across it. The anterior commissure felt normal. The membranelike structure posteriorly was torn by the finger, and the orifice would then admit the entire finger loosely. The regurgitant jet was still present but appeared to be less forceful. No thrombi were felt at any stage. The larger part of the atrial appendage was amputated, and the chest closed in a routine manner.

The postoperative course was smooth, dyspnea became less marked, and the systolic thrill disappeared. The murmur was much less evident. Digitalis was continued, and the child ate well and gained some weight. She was discharged home, clinically improved, three weeks after operation. Fluoroscopy, however, still showed a large left atrium. The child died suddenly at home, some six weeks after surgery.

Autopsy.—This was performed on the heart and lungs only. The specimens were obtained by the cooperation of Dr. J. M. Jauquet of Ashland, Wisconsin, and were fixed in formalin before examination.

The *heart* was large (Figs. 3 and 4), weighing 85 grams, both the right and left ventricles were thickened to 5 and 9 mm., respectively. The endocardium of the latter showed thickened whitish plaques when compared to the right ventricle. The wall of the left atrium was thickened (2 mm.) and the endocardium was white and opaque. The tricuspid, aortic, and pulmonary valves were normal. The foramen ovale and ductus arteriosus were closed. The coronary circulation, aorta, and great vessels were normal. The pericardial remnant showed evidence of inflammation, probably operative. The mitral valve circumference was 4 cm.; the diameter 1 cm.

Fixation had caused shrinkage, and the valve appeared incompetent when viewed from above. The leaflets were thickened and wrinkled, and the chordae tendineae so shortened as to be almost absent, with the papillary muscles inserting directly into the valve cusps. The valve had been cleanly split at the commissures.

The lungs were fixed, but showed no external anomaly. The pulmonary vessels were grossly normal with some evidence of atelectasis in both organs. A mucus plug occluded the lower trachea.

Microscopy.—This revealed infiltration in the subendocardial area with a thick mass of fibrous and elastic tissue. This was most marked in the sections from the left atrium and ventricle.

A diffuse cellular infiltrate with some intra-alveolar phagocytes was present in the lungs, and a few of the pulmonary vessels showed thickening. The histology supported the gross diagnosis of fibroelastosis.

DISCUSSION

The case here presented is an example in an infant of mitral stenosis, due to fibroelastosis. An effort was made to relieve the condition by finger-fracture of the mitral valve. The prognosis for the disease is generally agreed to be poor, and the partial success here encountered suggests that surgical intervention is justified, though complete preoperative investigation is a sine qua non.

The huge left auricle seen at fluoroscopy has been reported as a constant finding in seven cases of fibroelastosis of the left heart (Freer and Matheson[9]). The pulmonary capillary tracing did not suggest mitral regurgitation though this was in fact present and palpable at operation. This finding has been noted by Venner and Holling,[11] and Wynn and associates[12] found the left atrial pressure tracing to be similar in some cases of pure mitral stenosis and regurgitation. Baker and associates[13] have suggested that mitral commissurotomy is not precluded by mild incompetence, as the procedure may even relieve the condition to some extent. It would appear from the post-mortem specimen that the commissures were cleanly split, but that the valve remained regurgitant.

The etiology of fibroelastosis remains obscure. Day[1] and Eigen[14] considered it a fetal endocarditis but Gross[15] denied this. His opinion was that the basic lesion was a primary hyperplasia of the endocardial elastic tissue, with secondary infarction of the subendocardial muscles. Johnson[16] suggests that the cause is anoxia of the endocardium secondary to such conditions as anomalous coronary circulation, premature closure of the foramen ovale, and valvular atresia.

The pathology seemed typical of that reported by others[3,4] though the involvement of the aortic valve occurring in a case of Freer and Matheson[9] was absent. Bower and associates[4] note the difficulty of surgical approach where the left atrial appendage is small. This difficulty, fortunately, did not arise here, as the structure was capacious enough to allow full exploration and eventual amputation. The same authors comment, and we agree, that the risk of inducing regurgitation is preferable to a tight, untreated mitral stenosis.

SUMMARY

A case of isolated mitral stenosis occurring in a three and one-half month old infant is presented. The findings at cardiac catheterization, angiocardiography, and operation are recorded. The feasibility of mitral commissurotomy in this age group is demonstrated. A six-week survival with clinical improvement in the first month was obtained. The diagnosis and local results of surgery were confirmed post mortem.

REFERENCES

1. Day, H. B.: A Case of Mitral Stenosis Fatal at Two Years of Age, Lancet **1**:1144, 1932.
2. Johnson, R. S., and Lewes, D.: Advanced Mitral Stenosis at Three Years Old, Brit. Heart J. **7**:52, 1945.
3. Emery, J. L., and Illingworth, R. S.: Congenital Mitral Stenosis, Arch. Dis. Child. **26**:304, 1951.
4. Bower, B. D., Gerrard, J. W., D'Abreu, A. L., and Parsons, C. G.: Two Cases of Congenital Mitral Stenosis Treated by Valvotomy, Arch. Dis. Child. **28**:91, 1953.
5. Hellems, H. K., Haynes, F. W., Dexter, L., and Kinney, T. D.: Pulmonary Capillary Pressure in Animals Estimated by Venous and Arterial Catheterization, Am. J. Physiol. **155**:98, 1948.
6. Lagerlof, H., and Werko, L.: Studies on the Circulation in Man. VI. The Pulmonary Capillary Venous Pressure Pulse in Man, Scandinav. J. Clin. & Lab. Investigation **1**:147, 1949.
7. Gorlin, R., Lewis, B. M., Haynes, F. W., and Dexter, L.: Studies of Circulatory Dynamics at Rest in Mitral Valvular Regurgitation With and Without Stenosis, AM. HEART J. **43**:357, 1952.
8. Blumberg, R. W., and Lyon, R. A.: Endocardial Sclerosis, Am. J. Dis. Child. **84**:291, 1952.
9. Freer, J. L., and Matheson, W. J.: Left Auricular Enlargement in Endocardial Fibroelastosis, Arch. Dis. Child. **28**:284, 1953.
10. Zinsser, H. F., and Johnson, J.: The Use of Angiocardiography in the Selection of Patients for Mitral Valvular Surgery, Ann. Int. Med. **39**:1200, 1953.
11. Venner, A., and Holling, H. E.: Comparison of Operation and Clinical Findings in Mitral Stenosis and Incompetence, Brit. Heart J. **15**:205, 1953.
12. Wynn, A., Matthews, M. B., McMillan, I. K. R., and Daley, R.: The Left Auricular Pressure Pulse in Normals and Mitral Valve Diseases, Lancet **2**:216, 1952.
13. Baker, C., Brock, R. C., and Campbell, M.: Valvulotomy for Mitral Stenosis. Report of Six Successful Cases, Brit. M. J. **1**:1283, 1950.
14. Eigen, L. A.: Juvenile Rheumatic Fever. Report of a Case in an Infant Two Years of Age, AM. HEART J. **16**:363, 1938.
15. Gross, P.: Concept of Fetal Endocarditis: General Review With Report of Illustrative Case, Arch. Path. **31**:163, 1941.
16. Johnson, F. R.: Anoxia as a Cause of Endocardial Fibro-elastosis in Infancy, Arch. Path. **54**:237, 1952.

CURE OF ENTEROCOCCAL ENDOCARDITIS OF PROLONGED DURATION

DAVID KRAPIN, M.D.

NEW ROCHELLE, N. Y.

SUCCESSFUL treatment of *Streptococcus fecalis* endocarditis has been rare, totaling relatively few bacteriologic cures.[1-16] Of this number, one was presumed spontaneous.[8] Therapy of the others included a variety of drugs: neoarsphenamine, Mapharsen, enterococcus bacteriophage, Thio-bismol, penicillin, oxytetracycline, chlortetracycline, chloramphenicol, and streptomycin.

From this group, the combination of penicillin and streptomycin has had the greatest success. It was first used by Hunter[13] in 1947, and recently by Robbins and Tompsett[3] with notable results. The following case report presents a cure on concomitant dosage of penicillin and streptomycin. This followed approximately fourteen months of trial on several other suggested regimens and assumes significance because of its previous seemingly hopeless and protracted course. It is also deemed interesting in the light of survival of many complications, and the clinical symbiosis of host and organisms.

CASE REPORT

J. N., a 24-year-old housewife, was admitted to the New Rochelle Hospital, Feb. 25, 1951, for treatment of a spontaneous incomplete abortion. Examination revealed no cardiac murmurs, and the temperature, blood count, and urine were within normal limits. The products of conception were removed, she was curetted, and discharged one week after admission.

June 7, 1951, the patient was afflicted with acute pain at the base of the right second toe. Examination revealed no visible lesion. A harsh, Grade 3 mitral systolic murmur with a questionable early soft diastolic component was heard. One week later she developed a sudden, severe, sharp left upper quadrant pain, and a fever of 100.2° F. The sedimentation rate (Westergren) rose from 44 to 77 mm. per hour. The blood count showed 3.1 million red blood cells; 10.9 grams hemoglobin; 7,500 white blood cells (75 per cent neutrophils, 8 per cent nonsegmented). The electrocardiogram pictured nonspecific S-T segment changes. These symptoms gradually subsided, but left general weakness, increased fatigability, and headaches.

On July 6, 1951, a right-sided hemiplegia occurred. Examination revealed a blood pressure of 120/70 mm. Hg, regular sinus rhythm and a harsh Grade 4 mitral systolic murmur with a Grade 1 soft early diastolic. The fingers were slightly clubbed, lungs were clear, liver and spleen nonpalpable. The hemiplegia was complete. There was nuchal rigidity and motor aphasia. The sedimentation rate was 25 mm. per one hour (Westergren); red blood cells, 3.7 million per c.c.; 11.4 grams hemoglobin; 8,700 white blood cells per c.c. with 71 per cent neutrophils (10 per cent nonsegemented). Spinal fluid manometrics were normal, and the fluid contained one white blood cell, three red blood cells, 70 mg. per cent sugar, 15 mg. per cent protein, 679 mg. per cent chlorides. Throat culture grew *Streptococcus viridans;* urine culture, *Aerobacter aerogenes;* and blood culture, *Streptococcus fecalis.* The enterococcus was found very sensitive to chlortetracycline and oxytetracycline and resistant to chloramphenicol, streptomycin, and penicillin (disk method). No combination of antibiotics was more effective "in vitro" than any drug, alone.

Present address: 116 Petersville Road, New Rochelle, N. Y.

Received for publication April 1, 1954.

Therapy consisted of crystalline penicillin, 8 to 20 million units daily in divided doses, intramuscularly, or intravenously with heparin, and caronamide by mouth (according to the method of Loewe and associates[2]). A total of 557 million units was administered in a six-week period. In conjunction with penicillin, 128.5 grams of chlortetracycline and 146 grams of oxytetracycline* were given, though the latter two were not used together. Average dose was two to six grams daily. In addition, she received multiple blood transfusions and supportive therapy.

The temperature was 100.4° F. on admission but fell in three days and remained normal thereafter except for a two-day elevation to 100.2° F. noted during an episode of myocardial infarction. This occurred July 31, 1951, and was characterized by severe, crushing, precordial pain with left shoulder-to-hand radiation, apprehension, vomiting, a blood pressure drop from 110/70 to 90/60 mm. Hg, and the typical electrocardiographic changes of posterior wall involvement.

The course was further complicated by a small arterial embolus to the left groin. There was persistent vaginal bleeding of slight degree. Her paresis cleared rapidly and when discharged, Oct. 9, 1951, the motor aphasia had largely disappeared. She was able to walk with only a slightly hemiplegic gait and had limited use of the upper extremity. The mitral murmurs had not changed but a Grade 2 pulmonic systolic was present. The liver and spleen were never palpable and no petechiae were observed. Weekly blood cultures taken after the initial positive one on July 9, 1951, remained negative until discharge, Oct. 8.

However, the patient continued to have intermittent blood-tinged vaginal spotting and severe headaches. On Nov. 20 she had an acute episode of left flank pain and was readmitted to the hospital. Temperature was 99.6° F., blood pressure 100/80 mm. Hg, pulse 92. Her color was cafe-au-lait, spleen was not palpable, murmurs unchanged, finger clubbing minimal. Left costovertebral angle tenderness was elicited but urine was negative. The red blood count was 3.6 million; 76 per cent hemoglobin; 9,700 white blood cells (73 per cent neutrophils, 21 per cent nonsegmented). Sedimentation rate 41 mm. per one hour (Westergren). Blood culture grew *Streptococcus fecalis*. The sensitivity studies revealed penicillin 3.12 units; streptomycin, 50 units; chlortetracycline, 0.10 μg; chloramphenicol 4.30 μg; bacitracin 0.35 μg. On Nov. 21, 1951, the patient passed placental tissue containing clumps of bacteria with smear characteristics of a streptococcus. (Initial dilatation and curettage was on Feb. 25, 1951, with no normal menstrual cycle thereafter). Treatment consisted of 28 Gm. of oxytetracycline and 6 Gm. of streptomycin until discharge Dec. 18, 1951.

On Jan. 11, 1952 a positive culture was again reported. She was readmitted for hospital care. Physical examination revealed no change from the findings on Dec. 18, 1951. The sedimentation rate was 37 mm. per one hour (Westergren), blood count unchanged. The temperature was normal throughout her stay. Organism sensitivity to antibiotics had not altered.

Intensive penicillin treatment was instituted. The patient received sixty million units daily, intravenously, for twenty-three days to a total of 1.38 billion units. This treatment was prompted by the experience of Whipple.[18] The continuous daily infusion, in addition to penicillin, contained 50 mg. of heparin in 1,000 c.c. of Ringer's solution or 5 per cent glucose in distilled water. This was administered through a polyethylene tubing inserted into a vein. Because of the development of severe local thrombophlebitis at the infusion spot it was necessary to shift the tubing site every three days. Heparin did not forestall this reaction and the substitution of a needle for the tubing was not remedial. It was attributed to the irritative effect of penicillin.

Potassium penicillin (containing 5 Gm. potassium daily) was used initially but a blood level of ten[10] milliequivalents of potassium with electrocardiographic changes of toxicity was detected. This was not accompanied by clinical signs or symptoms, and after a balanced mixture of sodium and potassium penicillin was substituted all evidence of chemical imbalance disappeared.

Weekly blood cultures were sterile after the initial positive one on admission. The chest x-ray revealed no cardiac enlargement, and the ECG showed a stabile posterior wall myocardial infarction. Blood counts, sedimentation rates, and urinalysis remained unchanged to date of her discharge on Feb. 20, 1952.

On March 23, 1952, the patient developed signs of a small arterial embolus to the left calf muscle, and upon hospitalization was found to have a positive blood culture. This occurred

*Furnished by the courtesy of the Chas. Pfizer & Co., Inc., through Gladys L. Hobby, Ph.D.

despite daily doses of 3 to 5 Gm. of oxytetracycline and two weeks of daily intramuscular injections of 2 Gm. of dihydrostreptomycin, which were given following discharge in February. Examination revealed two ecchymotic areas 2 x 3 cm. over the left leg and ankle. This type of ecchymosis occurred intermittently throughout her stay despite sterile blood cultures and normal bleeding, coagulation, platelet, and prothrombin times. The spleen was not palpable, cardiac murmurs were unchanged, the clubbing was still minimal, and the temperature remained normal. The sedimentation rate was 45 mm. per one hour (Westergren); hemoglobin 13.1 grams; 7,600 white blood cells (18 per cent nonsegmented neutrophils). A blood culture, taken March 17, 1952, was positive for *Streptococcus fecalis*. Organism sensitivity studies revealed penicillin 1.56 units; streptomycin, 25.0 units; oxytetracycline less than 0.78 μg, chloramphenicol, 3.125 μg, chlortetracycline less than 0.39 μg; polymyxin over 100 μg; bacitracin, 3.125 units.

In view of the inability of the broad spectrum of antibiotics to eradicate the enterococcus completely, it was decided to try the combination of penicillin and streptomycin. Accordingly, the patient was given 10 to 20 million units of penicillin and two grams of streptomycin daily in divided doses, intramuscularly, (method of Robbins and Tompsett[3]) to a total of 1,154,000,000 units of crystalline penicillin and 105 Gm. of streptomycin (over a treatment period of approximately eight weeks).

During this therapy she developed oily deposits in both buttocks which resolved spontaneously. She protested bitterly at the frequent painful injections, but with occasional rests was able to tolerate the full course. Caronamide (Staticin), 4 Gm. every four hours, was given for approximately six weeks and was found to maintain the blood level of streptomycin at 500 units and penicillin at 400 units. Urinalyses during this period showed 4-plus albumin but reverted to negative with cessation of the drug. Blood urea nitrogen was normal.

The patient has been checked at frequent intervals since hospital discharge, June 9, 1952. Her hemiplegia has progressively decreased, and she now has good flexion function of the right upper extremity. The heart is not enlarged and reveals a Grade 4 mitral systolic murmur with no diastolic component. To date no signs of congestive heart failure have appeared despite normal activity. The sedimentation rate averages 15 mm. per one hour (Cutler); red blood count, 4 million, hemoglobin, 76 per cent. Ecchymotic areas in the lower extremities continue to appear intermittently with no adequate explanation. Blood cultures taken weekly for three months after discharge, then every two weeks for three months, and thereafter at monthly intervals have continued sterile.

COMMENT

This patient was afflicted with active *Streptococcus fecalis* endocarditis for approximately fourteen months and has since had clinical and bacteriologic cure. Her course illustrates several features common to infection with the enterococcus: the absence of significant fever, the relative symbiosis of organism and host over many months, the engrafting of infection on presumably normal heart valves, the portal of entry via urinary or genital tracts, and the absence of palpable spleen. The complications were multiple and included: peripheral arterial emboli, splenic infarction, hemiplegia, myocardial infarction, and deformed mitral valve. During treatment she developed oily deposits in both glutei muscles, thrombophlebitis at the site of intravenous infusions, and toxic quantities of potassium in the blood.

Her therapy covered all recommended and previously used agents except bacteriophage and the arsenicals. Each course seemed to subdue the organism, as shown by negative blood cultures, but eradication was difficult to achieve. It is noteworthy that only after the infected placenta was cast out was a cure obtained. This gives basis to the speculation that the endometrial implant was a source of infection to the heart valves. It would suggest that strenuous search for such foci in persistent or uncured cases be mandatory. A treatment failure in the series of Robbins and Tompsett[3] had multiple splenic abscesses, and it is possible that in such an instance splenectomy could be lifesaving.

The broad spectrum of antibiotics proved inadequate in this case, since, despite sensitivity of the organism and adequate dosage over long periods, the only accomplishment was temporary blood-stream sterility. The final *coup d'grace* was administered by a combination of penicillin and streptomycin. The effectiveness of this combination might well be ascribed to their synergism[17] since she had previously received single courses of 60 million units of penicillin daily for three weeks and 2 Gm. of streptomycin daily for two weeks, with relapse after each course.

SUMMARY

1. Some aspects of therapy in *Streptococcus fecalis* endocarditis have been reviewed.

2. A case report stressed the natural history of the disease, its protean course and complications, its resistance to treatment, and final cure with a combination of penicillin and streptomycin.

Dr. Harvey Collins, Bacteriologist, of the New York City Memorial Hospital, graciously contributed study and information to the bacteriology in this case. Dr. Ralph Tompsett of the New York Hospital contributed helpful advice towards therapy.

REFERENCES

1. Bader, M. E., Bader, R. A., and Friedberg, C. K.: Causes of Failure in the Treatment of Subacute Bacterial Endocarditis, J.A.M.A. **148**:1498, 1952.
2. Loewe, L., Candel, S., and Eiber, H. B.: Therapy of Subacute Enterococcus Endocarditis, Ann. Int. Med. **34**:717, 1951.
3. Robbins, Wm. C., and Tompsett, Ralph: Treatment of Enterococcal Endocarditis Bacteremia, Am. J. Med. **10**:278, 1951.
4. MacNeal, W. J., Blevins, A., and Poindexter, C. A.: Clinical Arrest in Enterococcal Endocarditis, Am. J. M. Sc. **211**:40, 1946.
5. Baehr, G.: Penicillin Treatment of Subacute Bacterial Endocarditis Due to Enterococcus, Regional meeting, Am. Coll. Phys. N. Y., Oct., 1944.
6. Harris, R.: Subacute Bacterial Endocarditis: Report of Enterococcal Infection Treated With Penicillin, Bull. New York M. Coll., Flower & Fifth Ave. Hosps. **8**:61, 1945.
7. Scrota, J. H., Gerber, I. E., and Baher, G.: Chemotherapy of Subacute Enterococcus Endocarditis, J. Mt. Sinai Hosp. **14**:604, 1947.
8. Bito Del Pino, S. A., Osimoni, J. J., and Digbero, J. C.: Acute Endocarditis Due to Enterococcus, Cured or in Unmistakable Remission, Arch. Urug. de med. Cir. y especialid **8**:383, 1936.
9. Zweifler, B., Sar, Eli, and Feder, Isodore: Subacute Bacterial Endocarditis Due to Streptococcus Fecalis, Ann. Int. Med. **34**:217, 1951.
10. Hein, Gordon, and Berg, B. M.: Recovery From Subacute Bacterial Endocarditis (Streptococcus fecalis), AM. HEART J. **38**:433, 1949.
11. Long, Perrin H., Schoenbach, Emmanuel B., Bliss, Eleanor A., Bryer, Martin S., and Chandler, Caroline A.: The Experimental and Clinical Use of Polymyxin, Chloromycetin and Aureomycin, California Med. **70**:167, 1949.
12. Harvey, John C., Mirick, George S., and Schaub, Isabelle G.: Clinical Experience With Aureomycin, J. Clin. Invest. **28**:987, 1949.
13. Hunter, T. H.: Use of Streptomycin in Treatment of Bacterial Endocarditis, Am. J. Med. **7**:436, 1947.
14. Naegele, C. F.: Streptomycin Treatment of Bacterial Endocarditis Due to Streptococcus Viridans: Report of Two Cases, Ann. Int. Med. **30**:1049, 1949.
15. Zeller, W. W., Hirsh, H., Dowling, H. F., Hussey, H., and Robinson, J. A.: The Treatment of Bacterial Endocarditis With Penicillin and Streptomycin, M. Ann. District of Columbia **17**:21, 1948.
16. Guss, J. H.: Successful Treatment of Subacute Bacterial Endocarditis With Streptomycin, AM. HEART J. **35**:662, 1948.
17. Robbins, W. J., Kavanagh, F., and Hervey, A.: Synergism Between Some Antibacterial Substances, Bull. Torrey Botanical Club **75**:502, 1948.
18. Whipple, R. L., Jr.: The Cure of a Patient With a Very Resistant Streptococcus Viridans Endocarditis With Massive Penicillin Therapy (Average Daily Dose of Eighty-six Million Units), AM. HEART J. **42**:414, 1951.

AORTIC SEPTUM DEFECT

REUBEN A. SPRENGEL, M.D.,* AND ALBERT F. BROWN, M.D.**

GLENDALE, CALIF.

AN AORTIC septum defect is a congenital malformation in which there is a communication between the aorta and pulmonary artery just above the valves. Collett and Edwards[2] in Type V of their classification refer to this abnormality as a congenital partial persistent truncus arteriosus with a localized defect in the aortic (trunco-conal) septum, producing a communication between the aorta and pulmonary trunk. This would appear to correspond to the case which we are reporting. Potter[6] refers to this defect as an incomplete or fenestrated truncus septum.

The embryologic development of the pulmonary artery and aorta and possible abnormal deviations are summarized by Potter:[6] ". . . partitioning starts between the fourth and the sixth aortic arches and progresses through the truncus toward the ventricles. The partition begins as a pair of elevated longitudinal ridges that arise on opposite sides of the wall, grow toward each other, and finally meet in the midline to form a complete partition dividing the truncus into equal parts, one of which is the aortic channel leading into the fourth aortic arches and the other pulmonary channel leading into the sixth aortic arches. The truncus ridges grow toward the ventricle in a spiral manner and the position in which they are found at their point of origin is reversed by the time they reach the level of the ventricles. This brings the pulmonary channel into communication with the right ventricle, and aorta into communication with the left ventricle." This normal division takes place between the seventh and eighth week of intrauterine life.[7]

Abnormalities that may occur are " . . . (1) failure of the truncus ridges to develop, (2) a local defect in the partition, (3) failure of the ridges to pursue a spiral course and (4) deviation from midline division with resultant decrease in lumen of the pulmonary trunk or the ascending aorta."[6]

These result in one or more of the following congenital defects: an aortic septal defect, a common arterial trunk, transposition of the great vessels. The aortic septum is continuous with the membranous portion of the ventricular septum which is the last part to close so that with an abnormal truncus septum there is almost always some associated interventricular septal defect.

Right ventricular hypertrophy accompanies aortic septum defect as a direct result of prolonged pulmonary hypertension which is caused by an atrioventricular shunt, severe pulmonary emphysema, and associated pulmonary vascular sclerosis.[7]

From the Department of Pathology, Glendale Sanitarium and Hospital, Glendale, Calif.
*Resident in Pathology.
**Chief of Pathology.
Received for publication May 3, 1954.

Clinical findings include cyanosis with clubbing of the fingers and toes, dyspnea, edema in the lower extremities, a systolic murmur in the pulmonic region, an inconstant diastolic murmur, and hypertrophy of the right and left ventricles.[3] An aortic septum defect should be suspected in the presence of an enlarged heart with right ventricular prominence, decompensation, and a systolic murmur at the pulmonic area; in other words, signs and symptoms suggestive but atypical of a patent ductus arteriosus. X-ray, electrocardiogram, and cardiac catheterization alone are not adequate for diagnosis. Thoracic aortography is the preoperative diagnostic method of choice.[4]

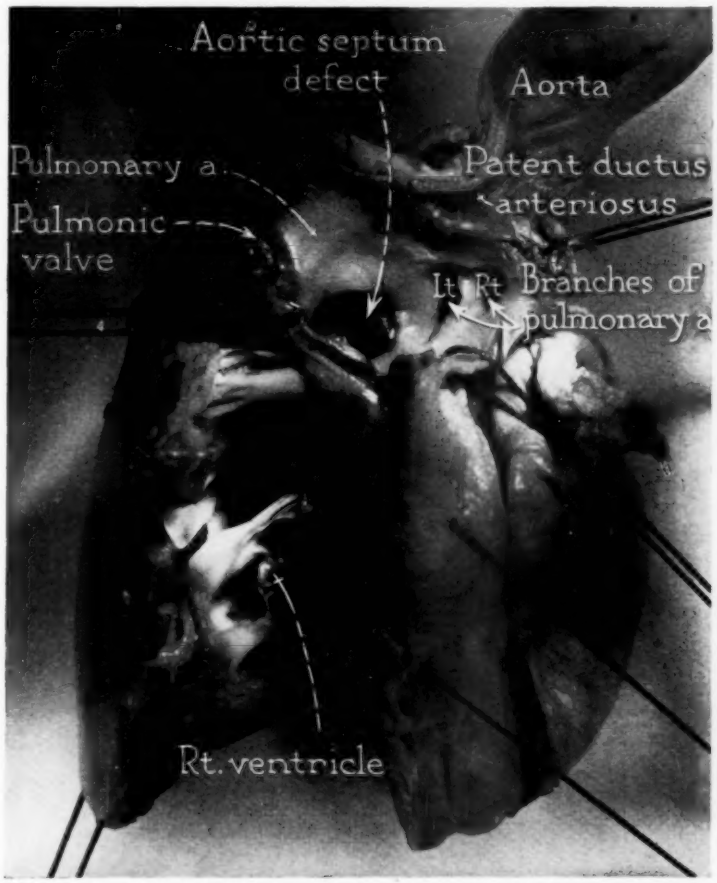


Fig. 1.—Anterior view of heart showing right ventricle opened, with aortic septum defect above the pulmonic valve.

When one congenital malformation is found, others should be suspected. Associated cardiac defects in reported cases of aortic septum defect are perforation of the pulmonic valves, patent ductus arteriosus, patent foramen ovale, bicuspid aortic valves with interventricular septal defect, and origin of the right pulmonary artery from the aorta.[3] In the case being reported there is an infantile coarctation of the aorta and a patent ductus arteriosus.

Differential diagnosis of this condition should include a shortened patent ductus arteriosus, an acquired type of communication caused by a rupture of an aortic aneurysm into the pulmonary artery, and an aneurysm of the sinus of Valsalva with rupture into the right heart.[7]

Death in most of the reported cases was due to congestive failure. Terminal cyanosis was due to a reversal of the atrioventricular shunt with congestive failure and advanced emphysema.

Downing[3] in 1950 reviewed the literature and compiled thirteen reported cases of aortic septum defect since early 1800. In the same article he reported another case of the malformation in a 9-year-old girl. Spencer and Dworken,[7] Adams and associates,[1] Downing and associates,[4] and Lanza[5] have each reported single autopsied cases. The instance which we are reporting brings to nineteen the total number of cases confirmed by autopsy.

The ages of the patients ranged from two days to thirty-seven years, and the defects, measuring from 2 to 16 mm. in diameter, occurred in the first few centimeters above the valves.

CASE REPORT*

Baby T., a white female weighing 2,850 grams and measuring 51.5 cm., was born on Aug. 16, 1953. The prenatal history was noncontributory. A frank breech delivery was accomplished without difficulty and respiration was spontaneous and good. On Aug. 18, 1953, the infant became extremely cyanotic and expired three hours later. *Autopsy summary* (significant findings only): The heart, though only slightly increased in weight (26 grams) appeared about twice normal size, due to ventricular dilatation, chiefly right. Immediately above the aortic valve (1.8 cm. circumference) and the pulmonic valve (2.8 cm. circumference) there was a 7-mm. communication between the aorta and pulmonary artery. Externally, for the first centimeter, the aorta and pulmonary artery appeared to form a common trunk. Above this level, a normal-appearing pulmonary artery gave off right and left branches and a patent ductus arteriosus. The latter was 1.5 cm. long and 1 cm. in circumference. The aorta as it formed a separate vessel narrowed from 2 to 1.5 cm. in circumference and gave off normal branches of the arch. An associated defect in this case was a congenital infantile coarctation of the aorta with pinpoint narrowing proximal to the ductus arteriosus.

SUMMARY

Congenital aortic septum defect has been discussed and a case reported bringing the total number of autopsied cases to nineteen.

REFERENCES

1. Adams, F. H., Diehl, A., Jorgens, J., and Veasy, L. G.: Right Heart Catheterization in Patent Ductus Arteriosus and Aortic-Pulmonic Septal Defect, J. Pediat. **40**:49, 1952.
2. Collett, R. W., and Edwards, J. E.: Persistent Truncus Arteriosus: Classification According to Anatomic Types, S. Clin. North America **29**:1245, 1949.
3. Downing, D. F.: Congenital Aortic Septal Defect, AM. HEART J. **40**:285, 1950.
4. Downing, D. F., Bailey, C. P., Maniglia, R., and Goldberg, H.: Defect of the Aortic Septum, AM. HEART J. **45**:305, 1953.
5. Lanza, G.: Sulle Comunicazioni Congenite Extrabotalliane tra l'aorta e l'arteria polmonare, Arch. Ital. Anat. Pat. **25**:331, 1952.
6. Potter, Edith L.: Pathology of the Fetus and the Newborn, Chicago, 1952, The Year Book Publishers, Inc., pp. 213-216.
7. Spencer, H., and Dworken, H. J.: Congenital Aortic Septal Defect With Communication Between Aorta and Pulmonary Artery; Case Report and Review of Literature, Circulation **2**:880, 1950.

*Service of E. D. Pratt, M.D., Burbank, Calif.